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The
Adrenal Glands
in Every-Day Medicine

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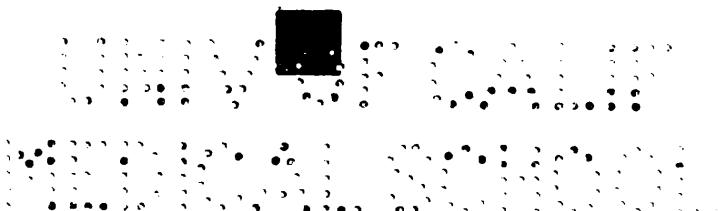


**The
ADRENAL GLANDS
in
EVERY-DAY MEDICINE**

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by Henry R. Harrower, M. D.**

The ADRENAL GLANDS
IN
EVERY-DAY
MEDICINE
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INTRODUCTION

Most physicians think of adrenal disease in connection with the name of Addison, the English physician who in 1855 described the adrenal syndrome which still bears his name; and knowing that this is a comparatively rare and fatal disorder, we are prone to give the matter scant attention.

Nevertheless the functional disorders of the adrenal glands are among the most important of all the difficulties encountered in the practice of medicine, for these little glands become functionally deranged much more commonly than we have been in the habit of believing. Then, too, their physiologic service to the body is so very important, that adrenal dysfunction, or dysadrenia, is of corresponding clinical importance.

The writer has written and collated a number of short items in an attempt to direct attention to the syndrome known as "hypoadrenia;" and it has been thought advisable to put these into a more compact and readable form. Hence this small brochure combining a number of articles and abstracts published in the little journal, "The Organotherapy Review." Of course there are repetitions and reiterations, but the subject is so fundamental and its clinical applications so practical, that this repetition may be an advantage.

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Without a doubt the routine consideration of the reaction of the adrenals to many every-day disorders, acute and chronic, makes a great deal of difference to the outcome of our attempts to cure them.

Glendale, Cal.

H. R. H.

March 1919

ASTHENIA: AN ENDOCRINO-NEURO- LOGICAL SYNDROME

**SHOWING THE INTIMATE RELATION OF THE
ADRENAL GLANDS TO NEUROLOGICAL
ASTHENIAS**

FRENCH medical men are more conversant with endocrinology than are American medical men. French medical literature contains more data on the subject, and therapeutic thought in France is far ahead of us, at least in so far as the internal secretions and organotherapy is concerned.

I have long promised myself that I would treat my readers to some more or less lengthy translations from French writers on endocrinology, and in going through the current (June, 1918) issue of *The Journal of Mental and Nervous Disease*, I find that there is a continued translation of Professor Laignel-Lavastine's work on "The Internal Secretions and the Nervous System," from which I will take the liberty of quoting several paragraphs, changing some of the translator's terms, since I am fundamentally opposed to such words as "thyroidal," "poly-glandular" (a hybrid, Greek-Latin combination), "hypo-physics" (when the word "hyposphyxia" was meant), and "endocrinial."

Asthenia is abnormal fatigue. It is either general or, more especially, motor or psychic.

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Motor asthenia is extremely commonplace, due to various causes—*infectious, toxic or psychic*.

Among the motor asthenias of endocrine origin, the first to be recognized was the asthenia of Addison's disease. It is connected with adrenal insufficiency, and is accompanied by arterial hypotension.

In addition there are motor asthenias allied with adrenal insufficiency which are not Addisonian. This fact is well known today. They are very common and usually, but not always, are accompanied by arterial hypotension. Their recognition and consequently their organotherapy will permit the cure of a large number of sick, ticketed as neurasthenics, cyclothymiacs, melancholics and even hypochondriacs. Certain cases of arteriosclerosis with hypotension enter into this category. The interesting point is that they were often asthenics already at the beginning of their arteriosclerosis, while they still had hypertension. This asthenia of hypertensive arteriosclerotics existing from the beginning, is well understood today. Maurice de Fleury was among the first to show its frequency. In such cases there is often a dyshyperfunctionating(!) of the adrenals. This asthenia of hypertension through dyshyperfunction may be recovered from completely through a simple regime. After a period of years it can border on asthenia due to adrenal insufficiency, an insufficiency itself secondary to the old glandular hyperfunction

and without the mechanical participation of cardiac insufficiency. I have followed a lot of such cases in the last ten years.

The majority of the endocrinogenous muscular asthenias are adrenal in their origin, but there are others which may be thyroid, thymic, parathyroid, pituitary, gonad or pluriglandular. Dejerine and Gauckler have added their weight of authority to support these data.

The endocrine origin of a muscular asthenia having been recognized, the diagnosis is not complete. The cause must be determined. In the simple cases it is sometimes an infection (a beginning tuberculosis, convalescence from grip or pneumonia, etc.) and in others it is an intoxication. In the more complicated cases it may be a vascular, nervous or psychic disturbance, under the subjection itself of a previous endocrine disorder. It is often like this in the "hyposphyxia" of Martinet, at typical case of which I have actually seen, which merits publication by itself.

An important fact is that the asthenia may not be the result but the cause of an endocrine insufficiency. Claude believes that this is the case in the paralytic myasthenia of Erb-Goldflam. According to him the endocrine glands are normal or rather increased in size, but they are functionally exhausted by a truly excessive effort. This is brought about by the entrance into the circulation of poisons of inconstant origin (but which occasionally may arise from a disordered thy-

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mus) which affect the nerve and muscle cells. In the Erb-Goldflam syndrome the multiple insufficiency of the endocrine glands (hypocrinism) by functional exhaustion is, therefore, secondary, just as the disappearance of the spongicytes in the adrenal cortex is secondary to an intense or prolonged muscular agitation. I have had occasion to confirm in eight cases this fact grasped experimentally by Mulon and clinically studied by Porak.

Remarks: M. Laignel-Lavastine is speaking of serious, neurological syndromes and he might well have included the temporary, "insignificant" periods of asthenia which are often ignored by the physician who reassures his patient and apparently satisfies his medical conscience with a "What you want is a good rest. Lay off your work for a while and take it easy. You'll be all right." This may be good practice, for obviously rest is the antithesis of fatigue; but to my mind it is not enough. As has been said, there is an important endocrine factor, the recognition of which "permits organotherapy treatment" and which, in Lavastine's own words, "permits the cure of a large number . . . ticketed neurasthenics, etc." Rest is negative treatment. It merely allows Nature to have a better chance. Organotherapy, on the other hand, is positive treatment, since it definitely encourages those endocrine organs which have been overworked, and actively favors the restoration of the deranged balance. Rest is good; but rest plus or-

ganotherapy is better; and quite the best of all is to add to these two essential measures, the removal as far as possible of every source of toxemia whether from a focal infection, from ingested poisons or from the alimentary canal.

My original enthusiasm for pluriglandular therapy originated in France. There they are in the habit of giving combinations of synergistic glands for the especial purpose of encouraging the all-essential functions of the endocrine glands which they are convinced are below par in all "run-down conditions." The French have shown us quite a few things—how to fight, how to stick, how to win. Now let us allow them to show us how to apply the fundamental principle of organotherapy in the treatment of a large class of functional dyscrasias, neuroses and asthenias.

THE SYNDROME OF HYPOSPHYXIA

A CIRCULATORY SYMPTOM WHICH ACCOMPANIES THE ASTHENIAS

IN the previous article Laignel-Lavastine refers to "a typical case of hyposphyxia which I have actually seen"—as though my good friend Professor Martinet, who discovered, identified and named this clinical syndrome, had been questioned by his famous colleague. I, too, have "actually" seen a case of hyposphyxia, and perhaps it may be well to devote a few lines to this comparatively unknown subject. The latest (Ninth) edition of Dorland's Medical Dictionary is the first to include this word. The definition there is "Hyposphyxia: a depressed state of the circulation, with lowered bloodpressure." It is indeed a common endocrine syndrome; and it was first brought into prominence by Professor A. Martinet, of Paris, late in 1912. (See "Une Syndrome Hyposphyxique," La Presse Medicale, Dec. 21, 1912, and "La Syndrome Hyposphyxique et L'Insuffisance Pluriglandulaire," Bull. Acad. de Med. de Paris, June 9, 1914.)

Briefly hyposphyxia is a modified form of asphyxia, hence its name. The stimuli which regulate circulation, cardiac efficiency and the blood pressure are deficient, the circulatory mechanism "lacks punch." This, it is believed, is largely due to a form of pluriglandular insufficiency in

which the adrenal element is prominent. Hyposphyxia, then, is closely allied to hypoadrenia.

From the standpoint of symptomatology it seems that the above position is perfectly reasonable. The principal clinical manifestation is circulatory insufficiency, similar to Lewis's "new syndrome" mentioned in an item in the August Issue of this little journal ("Neurocirculatory Asthenia," THE ORGANOTHERAPEUTIC REVIEW, August 1918, page 4). While the symptoms may not be identical, they are certainly quite similar: Poor circulation with bluish-colored and cold extremities, cardiac asthenia and hypotension, subnormal temperature and evidence of stasis due to poor circulation. With this invariably goes asthenia (due to poor cellular nourishment because of the bad circulation and, more important still, deficient hormone production with consequent reduced sympathetic function and generally slowed metabolism) and the usual findings of hypocrinism.

As a disease-picture *per se*, hyposphyxia is not common, for the good reason that other conditions so commonly accompany it that they are the ones that are seen and treated. I do not quite agree with Martinet that hyposphyxia is deserving of classification as a disease; but as an extremely important syndrome which complicates so many chronic disorders it is assuredly important and worthy of the same kind of study that our beloved French confreres have given it.

The treatment? The reduction of those in-

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sidious causative conditions which through toxemia or otherwise deplete the output of the hormones which regulate the circulatory department. The mechanical removal of stasis by means of massage, exercise, etc. The stimulation by means of homostimulative organotherapy of the glands which are largely at fault (whether as a cause or an effect). Good hygiene.

From my own particular standpoint, I know of no form of organotherapy better suited to the treatment of "neurocirculatory asthenia," hyposphyxia or the endocrine asthenias discussed in the item from Laignel-Lavastine which precedes this, than the pluriglandular formula which I call **Caps. Adreno-Spermin Comp.** It contains the adrenal principle—hypoadrenia is the rule in these syndromes. It contains a small dose of the thyroid principle which is complementary to the adrenin and stimulates oxidation. It contains spermin, the active principle of the interstitial cells of Leydig which is well-called "a cellular punch-producer." It increases circulatory efficiency, raises tension and is an "anti-asthenic remedy." Why should I not recommend it?

POST-INFLUENZAL ASTHENIA

SOME REMARKS ON THE RELATION OF "SPANISH FLU" AND OTHER INFECTIOUS DISEASES TO THE ADRENAL FUNCTIONS

THAT THERE IS a very well defined adrenal phase in practically every case of acute infectious disease is being discovered more commonly today than at any time in the practical study of endocrinology. It happens right now that the profession is beginning to connect adrenal dysfunction with many disorders and is studying the subject with much interest. Then along comes a real epidemic with thousands of cases, many of them serious, and it is natural for many to note the clinical symptoms in the broader light of our knowledge of this subject.

I was first led to consider the organotherapy of acute influenza, "Spanish" or otherwise, by some remarks made to me by a leading Oakland internist. I mentioned this in a short article in the November REVIEW. Since writing this and before its publication I began to get letters and telephone "visits" from a number of doctors who were connecting hypoadrenia with the "flu." I have been asked to tell more about this.

First of all let us recall what we have learned about the adrenals: (1) They regulate the sympathetic system, maintain muscular tone and blood pressure, and assist in supporting the chemical balance of the body; (2) They are very suscep-

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tible to all forms of toxemia, acute or chronic, exogenous or endogenous, and this toxic irritation first overstimulates and shortly depletes these glands functionally; (3) Adrenal depletion or hypoadrenia is therefore a **very common syndrome**, and its symptomatology is akin to that of organic adrenal disease—Addison's disease—though not near so serious and, of course, much more likely to respond to treatment.

The trinity of symptoms of hypoadrenia, acute and amenable to treatment or chronic and incurable as with the Addison syndrome, is this: **ASTHENIA, HYPOTENSION and MALNUTRITION.**

(1.) The asthenia is essential, the muscles are abnormally tired and cannot functionate. There is plenty of evidence to prove that there is a large element of neurasthenia and, most important of all, the tiredness is not limited to those organs which ordinarily are expected to become tired after work—the general cell chemistry is below par, elimination is poor, oxidation reduced and the glands of internal secretion are just as "rundown" as any other parts of the body. There is present a condition of **endocrinasthenia** or **hypocrinism** or pluriglandular insufficiency, as you may care to call it.

(2.) The hypotension is a part of the syndrome of "hyposphyxia" or circulatory insufficiency (hypotension, venous stasis, cold extremities and cardio-asthenia) which has been discussed in previous items in the REVIEW and is

fairly generally accepted as a definite clinical entity. In fact the reduced tension may be the first real clinical finding in hypoadrenia, whether functional or Addisonian. This lowered circulatory capacity with the blood pressure as the measurable factor is an undeniable thing. We see it every day—we measure it in actual figures—and nine times out of ten it is accompanied by the other commonly associated signs—fatigue or asthenia and varying evidence of malnutrition.

(3) The third symptom of the trinity,—malnutrition—is naturally not so prominent in an acute case, though it is surprising how quickly a patient will lose ten or fifteen pounds, a million or more red cells per cu. mm. and, generally, run down from the nutritional standpoint. Of course this is worse in chronic cases, and happens to be the most difficult and stubborn of the symptoms.

All of these symptoms of hypoadrenia are always present following a malarial chill, a dose of poison, an acute infection or any severe toxemia. The "let-down" in influenza, the serious hypotensive crisis in pneumonia or typhoid, the "algid stage" of cholera and the collapse following anesthesia are largely adrenal in origin, and many who are in a better position to know than I am call them adrenal pure and simple. There is also a growing weight of evidence to implicate the adrenals in severe mental conditions and, particularly, in "shell shock." I know, too, that several surgeons have applied this very idea as

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a routine following operation—as a means of reducing the effects of the “knock-out” given to the whole endocrine system by the anesthesia—and they say that it works fine!

Now, is this condition of adrenal depletion amenable to treatment? Assuredly, just as are other endocrine dyscrasias and for the same reasons. Naturally we first remove causes and from general principles we do all that our judgment indicates is advisable. We eliminate. We neutralize. We get after the focus of trouble if possible. We support. We sedate. Then, and in conjunction with all this, we start out to prevent and reduce the strain on the glands WHICH WE KNOW ARE GOING TO HAVE TO BEAR A HEAVY BURDEN. The ordinary measures are proper and helpful, but homostimulative organotherapy is of extreme additional service for we are going right to the seat of this particular phase of the trouble and applying the same well-founded principle of organotherapy that we use in every other condition in which we essay to prescribe glandular therapy. We can support the adrenal system and mitigate the results of its depletion. We can reduce the results of the depletion and prevent and forestall much of the asthenia that must inevitably follow the over-stimulation of these glands.

Does it work? The literature contains fully one hundred reports of the excellent results of the application of this principle in hundreds of

cases, acute or chronic—but, naturally, not of “Spanish Flu,” for there has not been time. However there are personal reports enough, and the fundamental philosophy of the thing is so obvious, to make me suggest that you try this out, for there are thousands of chances this very day. If you can reduce the most annoying “peplessness,” as one friend called it, and mitigate “the all-in condition” which hangs on for days and weeks after the actual infection, isn’t it well worth while?

Understand that this has nothing to do with the actual conditions of an infective nature, of prevention or even of cure. I merely assert that there is an endocrine phase to gripe, that it is properly called hypoadrenia, that the main symptoms of this endocrine phase are severe asthenia and a marked fatigue syndrome, and that suitable organotherapy prevents or materially lessens this.

WHAT IS THE SUGGESTED REMEDY? A combination long used for chronic cases of adrenal depletion and containing the adrenal principle to support the adrenal function, spermin the musculo-tonic and dynamic principle of the gonads, lecithin—the “most easily assimilated form of phosphorus” and a very small dose of thyroid. It is a pluriglandular tonic and I call it **Caps. Adreno-Spermin Co.**, and suggest that you prescribe at least 50, preferably 100 capsules —one q.i.d. beginning as early as possible.

HYPOADRENIA AND THE WAR

SOME EXPERIENCES WHICH EMPHASIZE THE CLINICAL IMPORTANCE OF ADRENAL DEPLETION

PERHAPS thirty papers and addresses have appeared in the last year or two relating to clinical experiences with adrenal substance and adrenalin in shell-shock, post-traumatic asthenia, collapse following antityphoid inoculation, hypoadrenia accompanying acute infectious diseases and, in general, emphasizing the importance of the adrenal functions in military medicine.

There is a great deal of practical helpfulness in some of the papers of Emile Sergent, of Paris, who for years has intensively studied the adrenal functions and, since the beginning of the Great War, has been successfully applying his ideas in military practice. For many years this writer has insisted that the adrenals played a much more important role than was admitted, and it is largely due to his efforts that our present knowledge and our clinical use of adrenal substance, has become established upon a solid and practicable basis.

Sergent has found innumerable opportunities to verify his previous opinions and experiences with the relation of the adrenals to various asthenic syndromes. His work at a base hospital in France (Bull. Acad. Med. Paris, Sept. 7, 1915) confirms the frequency of acute hypo-

renia following toxic-infectious influences, hemorrhage or shock. He calls particular attention to the possibility of individuals having a latent tendency to adrenal insufficiency which, under the stress of some acute toxemia, is suddenly aggravated with serious results. He encounters such conditions almost daily in sick and wounded men from the front.

In cases of this kind collapse is more likely to supervene in typhoid, influenza, pneumonia or other acute infections. **Sergent** uses adrenal substance as a prophylactic, and also many times has tided his patients over this dangerous phase with hypodermic or even intravenous injections of adrenalin.

Another French writer, **Satre** (Bull. Soc. Med. Hop. Paris, Dec. 28, 1917), reported some experiences with acute hypoadrenia in his military work. He had seen it following anti-typhoid inoculation and urges adrenal gland feeding in all cases where the beginnings of this condition can be detected.

Still another paper, by Drs. **Ramond** and **Francois** (Bull. Soc. Med. Hop. Paris, Oct. 8, 1917), concerns itself with a study of the disturbances of the adrenals resulting from the exigencies of war. Translating a statement we read: "This protracted war demanding of all our fighting men a continual moral and physical tension, forces overexertion on all the organs, especially the adrenal glands. The literature already con-

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tains manifold examples of weakness (asthenia), low blood pressure and (acute) dyspepsia from addisonism and in various acute infectious diseases. All bear the imprint of hypoadrenia. It is probably also an important feature in the clinical picture of the gassed." In their service in about four months they have seen no less than 26 cases of actual Addison's disease, all of which died save four, in which other factors, amenable to treatment with suitable gland feeding, were present.

In the same issue of the above journal Merklen draws attention to the frequency of hypothermia in military practice, especially in soldiers recovering from pneumonia or other acute illness. It is accompanied by extreme weakness and depression, and while this writer does not express himself decidedly as to the relationship of the adrenals to this condition, he mentions that it may be due to adrenal insufficiency. I confidently believe that it is, for in my own study of chronic hypoadrenia (in neurasthenia, pluriglandular insufficiency, etc.) low temperatures are extremely common, one case in particular having a temperature as low as 87 degrees F.

In a comparatively recent issue of American Medicine (Dec. 1915, p. 922) reference is made to Naame's work with cholera and dysentery. He believes that the adrenal element is quite the most important of all and that the so-called "algid stage" is nothing but an acute adrenal in-

sufficiency. Reference is made here to Sergent's experiences with this serious condition. Two cases of choleric form diarrhea were brought to the military hospital completely collapsed with absolute asthenia. One had for a long time shown symptoms of "an abortive form of Addison's disease," the other had recurring attacks of asthenia dating from a very severe typhoid fever some years before. Both cases showed the typical white adrenal line, extreme hypotension, reduced temperature and a decided tendency to collapse at the slightest provocation. Both were given adrenal treatment and rallied promptly under it. Following this report of Naame's and Sergent's experiences appears this pertinent statement:

"Incidentally this information is of just as great practical value in general practice as it is in the special conditions due to war. Hypoadrenia is not infrequent in the daily routine work and its relation to the severe forms of infectious disease is of extreme importance."

An important series of experiences reported by a Bordeaux physician and taken from a recent issue of the *Journal A. M. A.* is found on another page of this issue of the *REVIEW*. (See the item entitled "War Adrenal Insufficiency," elsewhere.)

ADRENAL DYSFUNCTION IN SANITARIUM PRACTICE

AN ATTEMPT TO SHOW THAT DYSADRENIA COMMONLY COMPLICATES SYNDROMES REQUIRING INSTITUTIONAL TREATMENT

WHEN an individual goes to a sanitarium or sanatorium it is usually because "ordinary medical attention" has failed to accomplish the desired results. Occasionally the general practitioner might have treated his patient at home as well as the sanitarium physician, but when conditions have become so chronic and of such long standing that the ordinary medical treatment needs to be supplemented with special diet, special office or bathroom treatment and special individual care which cannot be conveniently arranged for at home, both physician and patient are willing to try some institution. Generally speaking, the "sanitarium patient" is an old chronic case who has "gone the rounds" and is little or no better therefor.

No matter whether the case is in any of the several categories of disorders now best cared for in sanitariums—"mental and nervous," tuberculosis, drug or alcoholic or just plain "chronic"—they all have an endocrine phase which is worthy of careful consideration and treatment with the dietetic regulation, hydrotherapy, exercise, augmented elimination, and other institutional methods of treatment.

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Every physician in sanitarium practice will admit that toxemia is the greatest single cause of the various disorders he is called upon to treat, and whether this toxemia is the result of poor elimination, the ingestion of foods that are inadvisable, as coffee or improper amounts of proteins especially meats, the misuse of drugs or alcohol or of a focus of infection in the lung or colon or below the teeth or the tonsils or other usual places which may harbor a "focal infection," the toxemia is affecting more or less seriously every part of the suffering individual's body, including his endocrine system!

I will grant that the "sanitarium routine" is an advantage over the treatment usually adopted by the general practitioner, because the patient is ready to co-operate more thoroughly—is more in the mood because of environment, added expense and absence from home—in the necessary limitations in regard to diet, etc., and also because many of the physical or physiological methods of treatment in vogue in institutions have a broader influence upon the patient's deranged functions and go deeper to the root of their troubles. This is undoubtedly why sanitariums prosper and that patients come home shouting their praises.

I will also grant that my particular point of view prompts me to seek out and control as best I can disorders affecting the glands of internal secretion and I accept with pride the cogno-

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men "crank" which has occasionally been connected with my name. When I have a chance to "talk back" to some one who has called me a "crank about the internal secretions" I always tell them that "it takes a crank to turn wheels!" and that many of the world's greatest servants were "cranks" about their own particular work or interests. However, it is not "cranky"—or improper—to emphasize the importance of the endocrine glands and to give practical consideration to their functions or dysfunctions in connection with such other procedures of diet, elimination and hygiene that are obviously necessary.

I have repeatedly remarked that endocrinology and its corollary, organotherapy, fits in with every rational therapeutic procedure, and to study the effects of the endocrine derangements without considering the associated conditions, or to give glandular extracts without the other measures that circumstances call for, is the height of medical folly. I am frank to say that I think that the sanitarium physician who omits to give consideration to the endocrine side of his patients is missing a great deal; and on the other hand I KNOW that the sanitarium physician whose viewpoint is broadened to include a study of endocrinology as it pertains to his clinical work is daily rejoicing over the better results that his "sanitarium treatment" is securing when it is supplemented by treatment based upon the endocrine factors and

calculated to favor the reestablishment of disturbed ductless glandular function. THERE IS NOT A SHADOW OF DOUBT ABOUT IT.

Elsewhere in my writings I have laid stress upon the importance of the "minor" dyscrinisms, those insidious and overlooked derangements of function in the thyroid, the adrenals, the gonads, the pituitary and, in fact, all of the hormone producing organs. They are present in every sanitarium patient, and, too, usually are not taken into consideration at all. It is true that the underlying conditions of toxemia and deranged physiology are favorably modified by suitable "sanitarium treatment," and that gradually the removal of various sources of endocrine irritation permits a more nearly normal functioning of the all-important ductless glands; but this is what I call "negative treatment." The cause being removed, more or less gradually, the effects are allowed to take care of themselves. The same thing applies in the undoubted endocrine knock-out accompanying severe infectious diseases—the cause being controlled, the depleted glands are allowed to recuperate as best they can, thus prolonging convalescence and, time and again, permitting a relapse.

What I like to call "positive treatment" consists in doing more than removing causes and allowing Nature to do her best. I like to add to this, suitable support and boost the work of these little but by no means insignificant organs. And

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this can be done very easily and satisfactorily, too. Take, for instance, a case of slow metabolism with poor elimination, obesity and general cellular laziness. If they are given the added benefit of the "endocrine viewpoint," and a thyroid function test* is made and, possibly, a condition of latent hypothyroidism is noted, is thyroid therapy empirical in such a case? Not by any means; and, further, no matter how good the treatment, the diet, the environment and the skill with which you combine your "sanitarium methods," if your patient's thyroid capacity is below par they need thyroid, and it is the easiest thing in the world to give it to them. If you overlook this, and needed thyroid feeding is not given, the results cannot possibly be as good as though a grain or two of thyroid each day, reinforced or not as may be advisable, is added to your other excellent treatment.

The same thing applies to the sanitarium treatment of gynecological cases. If your patient is suffering from dysovovarism, how is your splendid routine regimen going to supply more of the ovarian hormone? It may in microscopical degree, by mechanically regulating the pelvic relations and circulation, but hundreds and

*A method of testing the apathy or sensitiveness of the thyroid gland has been developed in this laboratory (See "A Simple Therapeutic Test of Thyroid Function," New York Medical Record, Aug. 3, 1918, p. 196.), and further information, instructions and chart will be sent to interested physicians on request.

thousands of successes following the addition of ovarian feeding—best in my estimation by the use of a combination like my Caps. Thyro-Ovarian Co., which takes into consideration the fact that when there is dysovarism there cannot but be associated derangement in other intimately allied endocrine glands—prove that the fundamental principle of “homostimulation” is rational and resultful.

Quite the most important phase of what might be called “sanitarium endocrinology”—the application of these principles in sanitarium practice—concerns the effects of the causes of ailments that bring patients to you for treatment, upon the adrenal glands. We have agreed that toxemia is the greatest single factor. What does this toxemia do to the adrenals? To a pair of little glands that produce probably the most wonderfully active chemical in existence and that are subject to the slightest variation in the toxin-containing fluids that permeate them? The adrenals are known to control the sympathetic system, to regulate the automatic action of the complex blood-pressure-maintaining mechanism, and to influence many of the subtle chemical arrangements of the body. These I have outlined again and again elsewhere. Is not adrenal depletion a very obvious possibility in an individual with tuberculosis, where the insidious effect of the bacillary toxemia (added to the underlying nutritional disturbance, which to my mind is the real cause of the tubercle infection)

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is gradually hammering at the adrenals and depleting them and causing **hypoadrenia**? Are not the symptoms of adrenal depletion **asthenia, hypothermia, hypotension and malnutrition**? And are not these symptoms, probably in the above order, **pathognomonic of tuberculosis**?

Again, what about the neurasthenic? Toxemia is the great cause, dyscrinism the great effect. I recall an editorial in the Journal A. M. A. published a year or two ago entitled "Neurasthenia—Suprarenal Insufficiency," and an editorial in American Medicine based upon this and some pertinent opinions by Tom A. Williams of Washington, D. C. This is printed on another page and it emphasizes my own personal opinion* that the neurasthenic exhibits a perfect sequence of endocrine symptoms and that neurasthenia, of all conditions, deserves to be studied and treated as a condition in which **dysadrenia** is the most important fundamental factor.

What effect upon adrenal functioning should one expect to find following overdoses of poison when it is proved that these glands are invariably and seriously subject to the slightest changes in the content of poisonous substances, endogenous or exogenous, that reaches them through the circulation? Death from poisoning is commonly

*See especially Chapter IX, "The Relation of the Internal Secretions to Neurasthenia," in my book, "The Internal Secretions in Practical Medicine." (Sent on approval if desired.)

due to collapse. Collapse is an adrenal syndrome! Death from cholera—the algid stage—is said to be due to hypoadrenia; so is death from morphine or cocaine. Hence the morphinist has an endocrine phase worthy of consideration. Is there not also often a typical symptom complex of asthenia, malnutrition, hypotension and hypothermia? And the alcoholic, also?

Take the temperature two or three times a day of a hundred non-febrile sanitarium patients and it will be subnormal part of every day (and sometimes all day) in 80 per cent of them. Take their blood pressure and, excluding those with hypertension of organic origin—cardiac hypertrophy, renal disease, arteriosclerosis, etc.—and you will find it ranging from 80 to 110 mm. in more than half of them. Asthenia is their middle name! They have the fatigue syndrome with all its mental, physical and chemical disinterestedness, and are “tired to death.” Is this not the rule in Addison’s disease? In the convalescence from influenza? In the recovery from toxemia, acute or chronic, sudden or protracted?

I contend, with reason and the facts to back me up, that **Hypoadrenia is the most common single symptom in the gamut of cases that comes to a sanitarium for treatment**, that it is both a cause and effect of the other associated symptoms, and that it assuredly deserves attention equally with the other clinical manifestations. The treatment is more satisfactory when by means of suitable organotherapy the depleted

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adrenals are supported and their functional capacity enhanced. This materially stimulates fundamental cellular chemistry, and the increased blood pressure and generally increased vitality which follows indicated adrenal medication favors recovery and cooperates splendidly with the excellent measures constituting "sanitarium methods."

Pluriglandular therapy calculated to support the adrenals and simultaneously to increase oxidation and enhance cellular activity and nutrition, is being successfully used by a number of sanitarium physicians who have become interested in the work of my little "laboratory of applied endocrinology." The use of the formula Caps. Adreno-Spermin Co. has been attended with real success many times because: Its content of adrenin directly encourages waning adrenal function, spermin is a dynamogenic tonic which is obtained from the Leydig cells of the gonads, lecithin is a useful form of animal phosphorus and a small dose of thyroid completes what I confidently recommend as a really useful endocrine tonic. It raises abnormally low blood pressure—in actual, measurable figures. It imparts a feeling of well-being due to the increased hormone action undoubtedly brought about by its several ingredients. It has raised a pathologically low temperature more than once—in figures. Adrenal support by means of this particular formula is indeed a splendid measure.

THE DIAGNOSIS OF HYPOADRENIA

SOME POINTS ON THE SYMPTOMATOLOGY OF SYNDROMES OF ADRENAL ORIGIN

THE special attention which is being accorded to the importance of adrenal insufficiency in connection with the "let down" accompanying influenza, has prompted several correspondents to ask for more information, especially about the diagnosis of this condition.

Hypoadrenia, or functional depletion of the adrenal glands, is easily diagnosed. The outstanding symptom is ASTHENIA. The muscles are tired, the heart action is weak and the sounds indicate that this organ is lacking in "punch," there is a pronounced psychasthenia, the chemical processes of the body are reduced with corresponding findings in the urinary solids and especially the urea. As a result of this cellular asthenia, we have increased toxemia and a vicious circle is formed. The undue production of wastes, all of which are "alkali robbers," neutralizes a large share of the organism's reserve of alkaline mineral salts and the condition called "demineralization" is present. Sometimes this is called acidemia or acidosis, and whatever the name or degree, alkalies are a God-send and should be given carefully but generously.

The best way to measure the degree of cardiac asthenia is to take the blood pressure which is pathognomically low in all cases of hypo-

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adrenia, in fact this may be the first obvious evidence of adrenal insufficiency.

Still another diagnostic symptom is usually present, no matter whether the case is of acute or chronic origin. Malnutrition is the rule. Loss of weight occurs rapidly in acute conditions—it is no unusual thing for a short siege of influenza to be accompanied by a loss of 10 or even 20 pounds in weight—and more slowly in the long-drawn-out chronic adrenal insufficiencies as in tuberculosis, hepato-biliary insufficiency and abdominal ptosis.

Hypothermia is a fourth usual symptom. The temperature is routinely subnormal. This may be due to the circulatory insufficiency (hyposphyxia) or to the lessened metabolism or nutrition. Whatever the cause, it is very commonly present, in the acute cases following the period of hyperpyrexia (subnormal temperatures are very common after influenza or pneumonia) and in the chronic cases one finds it coupled with the usual asthenia and hypotension. I have not a doubt that the hypothermia of tuberculosis, like the early and pathognomonic asthenia, is of adrenal origin or, if some of my friends prefer not to say this so straightly, "is a part of a syndrome in which hypoadrenia plays an important part!"

The symptomatology of Addison's disease is identical, differing only in degree and curability. Here, of course, there is a definite destruction of the adrenal tissue and, so far as we know, this disease is incurable, despite the fact that the in-

dicated gland feeding often makes a remarkable change for the better.

An interesting point in the diagnosis of hypoadrenia is concerned in the reaction of the patient to suitable organotherapy treatment. After a few days (in acute cases) or weeks (in chronic cases) the asthenia is noticeably less, the early morning fatigue and the mental depression is reduced, the blood pressure is higher and there are obvious evidences of awakened cellular activity. This applies with greater force to functional cases than to Addison's disease, but even here the results of adrenal feeding are remarkably good, even though temporary.

Whenever you encounter hypotension, asthenia, an abnormally low temperature and cellular apathy you can very properly call it hypoadrenia, especially when previous circumstances have been of such a character as to overstimulate and, therefore, deplete these all-important little regulators of the sympathetic affairs of the body.

THE "WHITE ADRENAL LINE"

SERGENT'S VASOMOTOR PHENOMENON OF DIAGNOSTIC VALUE IN HYPOADRENIA

A NUMBER of years ago, Emile Sergent, a Parisian physician who has done much to emphasize the importance of dysadrenia and has written many articles and books on the subject, discovered a peculiar vasomotor phenomenon which has been developed as a useful diagnostic sign of adrenal insufficiency. I have sought it as a routine for some years, and have found it a reliable diagnostic procedure in all cases of organic adrenal disease (Addison's disease) as well as in the serious functional hypoadrenias. It is not likely to be seen in slight and temporary conditions of adrenal depletion. As a diagnostic adjuvant it is indeed useful and a few remarks as to the method of its interpretation may be profitable. The following statements are based on a paper by Sergent published in "Endocrinology" for January 1917:

The so-called "ligne blanche surrenale" is elicited by outlining a square or other figure upon the abdomen with a blunt object, as the rounded end of a fountain pen or the finger tip. Care should be taken to avoid rubbing, especially with the nail. Simple superficial stroking is used, do not bear down or scratch. After, say, half a minute, a pale line or band begins to be noticed following the course of the pen or fin-

ger. Gradually this becomes more and more distinct and white and larger, so that eventually the line is larger than the actual area stroked. This white line attains its maximum clearness in about one minute and lasts for from one to three minutes. This applies to "the well-defined cases of adrenal insufficiency, the only ones, in fact, in which this test has any real value."

Sergent believes that this phenomenon is the result of the hypotension which accompanies the hypoadrenia, and suggests the following explanation: "In arterial hypotension we know that there is a peripheral vaso-dilation; if we begin to produce a light stimulation of the skin, vaso-constriction will replace the vaso-dilation." Sergent very properly warns us against a tendency to "seek the absolute in clinical medicine." We know that clinical procedures are only approximate, and that no single test or symptom is absolute or incontestable evidence. We strive rather to group signs and syndromes and to associate them with the results of functional action and reaction. When a "white adrenal line" is seen it should quicken the attention to note other signs of hypoadrenia—hypotension, asthenia, melanoderma, hypothermia, etc. Any or all of these may be present, though the discovery of one of them, the pigmentation, for instance, is not an absolute sign since it may result from other conditions than the typical Addison syndrome.

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While Sergent's method outlined here was first announced several years ago, it does not seem to have attained much popularity in this country, though it is occasionally referred to in French journals. Despite this, this measure may be of much value especially, for instance, in studying serious symptoms-complex following the acute infectious diseases. The test as here described has the advantage of extreme simplicity and convenience, plus a diagnostic value which is most serviceable.

This measure is not infallible. It merely supplements other clinical findings or stimulates our diagnostic search, as the case may be. It is a simple and altogether worth-while procedure, worthy of routine application in the study of all asthenic states and, in fact, in a majority of the chronic disorders.

PLURIGLANDULAR THERAPY IN ASTHENIA

EVIDENCE TO CONFIRM THE VALUE OF REINFORC- ING ADRENAL MEDICATION WITH OTHER EXTRACTS

AS I have been looking through my clippings and journals to add weight to the evidence which I propose to lay before the readers of the REVIEW in regard to the importance and treatment of adrenal depletion, I am really surprised at the amount of data there is to establish and sustain our faith in pluriglandular therapy. From time to time some of these articles are abstracted here. There are many more. I urge the clinical study of this subject, for I know that the results excel those expected from the use of single products alone. My own work has been largely with endocrine dystrophies, nine-tenths of which are chronic; but recently (during the influenza epidemic) I have both seen and heard of remarkable results from pluriglandular therapy in acute cases.

Several have asked my why I am not satisfied to give adrenal substance alone, and my reply has always been because the adrenals are not disturbed to the exclusion of the other endocrine glands, and what will seriously affect one gland in the endocrine chain, must needs also affect some or all of the others. Personally I reinforce plain dessicated adrenal gland because

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I have tried it alone and with many varying combinations and have seen better clinical results from the combinations. This is empiricism, I admit; but why draw the line there when the results are real and even measurable by accurate instrumental diagnostics? The thermometer, the sphygmomanometer and, if you can get it, the ergograph all show that pluri-glandular therapy is a tonic, stimulant measure.

I add spermin to the adrenal substance indicated in hypoadrenia, because this active principle from the testes has a remarkable musculo-tonic and dynamic effect. And in hypoadrenia there is a predominance of asthenia, or muscular fatigue. The lecithin is merely a useful form of phosphorus which is theoretically useful and may be responsible for at least a small part of the general benefit. Assuredly the small dose of thyroid exerts a large influence for good, not merely because so often the addition of thyroid to other gland extracts "seems to act as Worcestershire Sauce brings the flavor out of meat," but because when there is hypoadrenia there is also hypothyroidism, the two go together very commonly, just as these two endocrine products reinforce one another.

I have used formulas quite similar to that now called Caps Adreno-Spermin Co. in various forms of asthenic, run-down conditions for several years. I like the effects. The other day I discovered an abstract (Journal A. M. A. Feb 2, 1918; p. 350) by a French physician which shows

that others besides myself believe in combining adrenal, thyroid and gonad extracts.

In a paper considering the excessive fatigue so often seen in men at the front, Cheyrou (Le Progres Medical, Nov. 10, 1917) says that the nervous system shows the effects of this fatigue markedly. The "asthenic syndrome," scarcely considered before the war, is very prevalent and with this is a decidedly lowered resistance to infection. As fatigue reduces the alkalinity of the blood, the alkaline minerals should be supplied artificially, with, of course, laxatives to keep the emunctories open. Occasionally Cheyrou gives strychnia "to reinforce the nervous system" and recommends adrenal extract "to restore muscular tone." He states that the administration of adrenal substance has aided materially in overcoming asthenia and hastening the elimination of toxins. Extract of the gonads (containing spermin) may be given with it together with means to recalcify the organism.

It is remarkable how closely the above suggestions come to the formula which I use, which, by the way, also contains the glycerophosphate of calcium as a therapeutically active filler. When I read this article it almost seemed as though Cheyrou had been using and was referring to my own formula; but he was not.

Since the fatigue syndrome and the symptom-complex of hypoadrenia is so very common in all phases of practice, one cannot go far amiss by giving due consideration to the adrenal side.

ADRENAL SUPPORT IN INFLUENZA

CLINICAL EXPERIENCES ESTABLISH REASONABLE- NESS OF PLURIGLANDULAR THERAPY IN POST-INFLUENZAL ASTHENIA

TWO MONTHS ago it was suggested in these pages that the adrenal functions were involved in influenza, pneumonia and other acute infectious diseases, and that adrenal support was in order as a part of the treatment.

Many clinical experiences have established this since, and there is no longer any doubt that the adrenals deserve careful study in this extraordinarily prevalent disease. Here are some facts which repeatedly have been established—at least in my own mind:

1. The blood pressure is low following influenza.
2. The severe asthenia or "let-down" which characterizes this disease, and especially convalescence from it, is a part of a syndrome so nearly identified with hypoadrenia that it is not unfair to call it by that name.
3. The circulatory insufficiency that accompanies influenza—the hypotension, subnormal temperature, venous stasis and cardiac asthenia or "hyposphyxia" (Martinet)—is the chief predisposing cause of the serious and all-too-common sequel, pneumonia. (Poor circulatory efficiency with stasis certainly does not favor resistance to the pneumococci or any other germs.)

4. Attempts to make these facts of service establish as fully as sphygmomanometry the rationale of this conception. In other words the success which follows adrenal support emphasizes the importance of the adrenal depletion.

I have personally seen and heard enough to convince me absolutely. In the cases I have seen myself every single one had a decidedly low blood pressure. Only one was normal—120 mm.—and when I got home I mentioned this to my wife as though it "spoiled the uniformity of my series;" but next morning the tension was only 90 mm.! I have seen varying degrees of severity, from post-influenzal pneumonia in a mother six months pregnant (b.p. 78 mm.) to a simple febrile disturbance with a little aching of back and limbs. To all I have given generous doses of alkalies and adrenal support. (To the pregnant mother I gave 15 minims of adrenalin solution under the tongue every hour for a while, with frequent cool alkaline enemas and as much sod. bicarb. as I could get her to take. Both she and her baby are "still alive and kicking strong!")

All these patients received varying doses of my Caps. Adreno-Spermin Co., usually 4 capsules a day, one or two received 5 capsules, 1 every 3 hours; and several of them remarked that there was "something in those capsules that helped me a lot."

Of course these experiences have not been

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limited to my own practice. Dozens of colleagues have written me in terms of warm encouragement. Still more have seen me in the office or on the street or have telephoned to me, and many expressions of enthusiasm have encouraged me mightily. Most of these remarks are quite colloquial, but they lose nothing by being passed on as near verbatim as possible as I jotted them down at the time:

"You are quite right about the blood pressure in flu. I haven't failed to find it low—below 100, as low as 70. Your Adreno-Spermin stuff is fine. I took it myself!"

"Funny we haven't been on to this thing before. I've always known that adrenalin raised blood pressure, but my experience in this epidemic has shown me how important this is. I am indebted to you for showing me this. I am using your Adreno-Spermin formula every day."

"There sure is some pep in your 'Number One.' I have been surprised how promptly it works in the low pressure which I see every day in influenza."

"I have been using your A. S. Co. during the epidemic and have gotten some fine results thus far. Both myself and wife convalesced on it."

"Yes, I really believe that I have saved lives with this formula. I am certain it does something very useful in these cases."

—And so on. This is not hot air, nor is it sales-talk. It is an expression of confidence engendered by splendid experiences following the application of an idea that to many physicians is almost new and untried. Elsewhere in this issue is a further explanation of the principle involved and why this measure ought to be an effective treatment where adrenal insufficiency is present or anticipated.

CLINICAL EXPERIENCES

From month to month there appear in current medical literature articles drawing attention to experimental or clinical experiences which broaden our view of the adrenal glands as large factors in many phases of the practice of medicine and surgery. A number of these have been abstracted and briefly commented on in issues of "The Organotherapy Review" and it has been thought that it would be helpful to reprint several of them to round out this little book:

THE ADRENAL FUNCTIONS

Professor H. Roger, of Paris, has done much research recently on the functions of the adrenals and in a comprehensive study of this subject reviews the multiple functions of these glands. They participate continuously in the workings of the economy and respond with remarkable rapidity to different nervous and toxic excitations. They have the capacity of restoring almost instantly the balance in the blood pressure, or at least counterbalance the morbid influences which tend to depress it. They intervene as well in psychic disturbance as with material nerve lesions; and combat the exhaustion of the heart induced by fatigue, modifying the action of the pneumogastric on the heart. The adrenals also regulate nutritional metabolism and influence the consumption of sugar. They serve in the elaboration of certain pigments, of cholesterol and of some of the lipoids, and seem to exert a destructive action on different poisons formed or introduced in the organism. This multiplicity of functions explains the numerous disturbances for which adrenal dysfunction may be responsible; and also lends emphasis to the importance of their more thorough consideration in routine practice.

According to Roger the adrenals play a very definite role in the development both of hypertension and arteriosclerosis, both clinically and experimentally (for many experiments were performed in rabbits and artificial arterial sclerosis was often produced). It is also remarked that the pancreas hormone antagonizes the action of the adrenals.—*La Presse Medicale*, Nov. 22, 1917.

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Remarks: All of which adds weight to our opinions about the all-essential function of the adrenal glands, especially in acute or chronic toxemias of varying origin; and, too, it gives a further scientific basis for the work we are attempting to do in the development of an organo-therapeutic remedy for functional (adrenal or toxic) hypertension. Parenthetically I have made a few remarks about some splendid clinical results from this form of treatment in "The Editor's Personal Pages" of this issue. Read them and get enthused!

ADRENAL INSUFFICIENCY IN NEURASTHENIA

The glands of internal secretion are being connected with the causation of the neurasthenic syndrome more and more frequently, and rightly so. Recent confirmation of the position taken in our editorial columns that "it would appear that the organs of internal secretion are to be charged with causing many of the disorders which together cause the neurasthenic syndrome" is found in an article on "Therapeutics" in the Journal of the American Medical Association entitled "Neurasthenia—Suprarenal Insufficiency" (Dec. 18, 1915, p. 2166).

According to Tom A. Williams the syndrome of adrenal insufficiency is really a form of nervous prostration, or as it has been called in more recent years, the fashionable "neurasthenia." The typical neurasthenic generally, if not always, has a disturbance of the adrenals on the side of insufficiency, the blood pressure is almost always low and the circulation poor. Mental exertion often causes extreme weariness and exhaustion. There may be a vasomotor paralysis which causes chilings, flushings, cold or burning hands or feet, drowsiness when the patient is up and wakefulness on lying down.

It is believed that many individuals presenting the classical symptoms of neurasthenia with low blood pressure, decreased mental elasticity, mental and physical depression with the fear that they cannot now accomplish their usual good mental work, with the story that they have "lost their nerve," with a vacillating and indecisive frame of mind, are suffering from functional hypoadrenia. In many cases of this character Williams has found that two to four grains of dessicated adrenal gland, three times a day, has caused improvement, and the administration of this substance by mouth has frequently raised the blood pressure as well as controlled the physical and mental derangements.

It must also be remembered that the typical neurotic very often has a disturbance of the thyroid gland and this in one patient may cause hysteria and in another depression; or both conditions may occur in the same patient at different times.

There is not much doubt that the cause of neurasthenia is a disturbance of one or more of the internal secretions, but just which glands are at fault is difficult to determine. Testicular and ovarian disturbance, especially on the side of deficiency, are known to cause general depression, hysteria, hypochondriasis, melancholia and digestive disturbances. In fact, as has been repeatedly stated, in "run-down conditions" of which neurasthenia is a typical example, one must expect a pluriglandular insufficiency; and under such circumstances Williams's suggestion to use total adrenal gland may well be amplified and thyroid, pituitary or gonad extracts given as the circumstances indicate. The value of pituitary medication is especially emphasized, Williams remarking that this gland furnishes a stimulant to the adrenals and hence "it might be well to consider administering a small dose of this gland in conditions of subsecretion of the adrenals, especially as part of the pituitary furnishes a vasopressor substance."

It is confidently believed as our clinical experience is extended and the suggestions made here and elsewhere are put into practical use, that we will find organotherapy of considerable efficacy in the successful control of many of the manifestations of neurasthenia.—American Medicine, March 1916.

Remarks: The direct suggestion to consider neurasthenia as an endocrine syndrome, and to use adrenal therapy, which "may well be amplified by thyroid, pituitary or gonad extracts," is quite in harmony with my own ideas which are embodied in the pluriglandular formula containing all of these glandular substances.

THE ADRENAL GLANDS IN PNEUMONIA

Pneumonia is beginning to be well known as more than a pneumococcal infection with severe toxemia, it is a circulatory disturbance and as such the study of the factors calculated to influence the circulation and the use of remedies which control the work of the heart and blood vessels, are likely to produce more satisfactory results than the other treatment alone.

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If one estimates the blood pressure in a dozen or a hundred cases of pneumonia no matter whether well-advanced or in the "threatened pneumonia" stage, as a rule it will be 110 mm. or less—more than often, less. The blood pressure is reduced. The heart is working overtime and its rate is excessive, a pulse of 120 or more is usual. The temperature is high.

There is no case of pneumonia in which the function of the adrenal system is not deranged. It is impossible for the sudden and extreme toxemia not unduly to stimulate these important glands, with an eventual hypoadrenia. This adrenal depletion is more serious than the preceding hyperadrenia, for when there is an excessive liberation of adrenin it is quickly oxidized and practically the only symptoms of the temporary adrenal excess are sympathetic irritability, cardiac excitability and a dry mouth and throat.

The hypoadrenia is both the precursor and the cause of circulatory weakness, collapse and death; and it begins to manifest itself much earlier than one has been accustomed to think. The adrenals are overburdened in the earliest stages of pneumonia—even before it is clinically possible to make an absolute diagnosis of this disease.

Obviously the essence of good practice in the treatment of this protean disease is to attempt to forestall complications, and adrenal insufficiency is the complication which is most common, most serious and most often overlooked and ignored. To prevent adrenal depletion is not the easiest matter but, at least, it is indeed a step in advance to realize that there is such a thing, and to watch the pulse arterial tension with vigilance. Supportive organotherapy is certainly worth while, either adrenal substance or a pluriglandular combination calculated to homostimulate "the adrenal system."

WAR ADRENAL INSUFFICIENCY

Carles, writing in the *Journal de Medicine de Bordeaux* (July 1918), tells of having seen within the last year fifteen cases of what seemed to be Addison's disease, in men on active service, except that it displayed a tendency to spontaneous subsidence, even in the apparently gravest cases. A few weeks of rest and quiet, abstention from meat, and treatment with adrenal substance soon banished all the symptoms. In two of the cases

there was what Loeper has described as adrenal dyspepsia notably improved by adrenal medication. The symptoms developed in all after a period of exhausting fatigue, an infectious disease, or gassing. The asthenia was the most striking symptom, more mental than physical. For months the men were incapable of reading a paper, writing a letter or even answering questions that required any thought. Improvement in this respect was rapid under adrenal treatment. The blood pressure was low, but according to Carles this is common among all the men at the front. A certain tendency to bronzing of the skin was perceptible in all the fifteen cases. The adrenal glands after recovery are left below par, and resumption of active service is likely to rearouse the old trouble, and the next time it might prove grave beyond recuperation.—Journal A. M. A., Sept. 7, 1918.

Remarks: Particular importance is laid on the cause of these cases of severe hypoadrenia, it is similar to the origin of many cases in civil practice, the difference being only one of degree. The condition of adrenal insufficiency, where these glands are "below par," is extremely common and it only takes a short period of toxemia from any cause, such as, for instance, an acute infectious disease, or a severe mental shock, to "knock out" the adrenals quite seriously. In such cases prophylactic adrenal support is indeed in order. Especial interest attaches to the remark that hypotension is the rule in men in the trenches, the mental and physical stress probably being responsible for the hypoadrenia, in accordance with the researches of Cannon.

ALKALIES IN INFLUENZA

In a short article in the Journal A. M. A. (Oct. 26, 1918, p. 1431), Ely, of Philadelphia, states that it is universally agreed that in perverted metabolism by bacterial invasion, it is the acidosis that is fatal. When the system is well alkalinized there is poor soil for bacterial growth. The baneful acids may be neutralized by harmless alkaline salts which seem to act almost specifically. Ely reports "a very successful experience" in the epidemic of Spanish influenza during which he had to see as many as one hundred private patients a day, and the results cannot be dismissed as accidental or unique. He states that the administration of these mineral salts "seems to represent an important new medical fact (!), or one for-

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gotten or generally overlooked." This remineralization is without any possible objection and its routine use is strongly urged.

Remarks: This procedure is indeed life-saving, for it not merely neutralizes the acid wastes which are always in such excess in acute disease (and, for that matter, in most chronic ones) but replaces the essential mineral reserve of the body which is so necessary to the maintenance of a normal cellular chemistry. My own reiterations about remineralization by the use of a combination of the salts in proportions quite similar to those in the blood are in exact harmony, in theory as well as in practice, with Ely's pertinent remarks.

Many scores of my friends are now prescribing my **Tab. Calcium Phosphorus Comp.** in 2 or 3 gram doses, crushed, with generous amounts of water, remote from food, two or three times a day. It is good in influenza or in hyperthyroidism; in rheumatism or in hypoadrenia; in fact where there is toxemia, present or prospective, the endocrine glands are or will be deranged and the saving mineral salts are used up too fast, hence pluriglandular therapy is properly reinforced by remineralization.

HYPOADRENIA AND ANTI-TYPHOID INOCULATION

In an abstract from a Colombia medical journal (see *Journal A. M. A.*, October 26, 1918) on some experiences with vaccination against typhoid fever, Mendez remarks about the importance of adrenal insufficiency as a contraindication for inoculation. His opinions are based largely on an extraordinarily severe reaction in a case of this type which was cured by the injection of adrenalin solution. Mendez believes that it would be of advantage to note whether major findings of abnormal adrenal functioning are present and, if necessary, to use preventive treatment first.

Remarks: Several French writers have discovered this in their army work, and at least two of them urge the segregation of the hypoadrenic type for preliminary treatment with adrenal organotherapy, using the blood pressure and temperature as the principal indicators. Incidentally the reaction which occasionally accompanies anti-typhoid inoculations is similar in symptomatology, as well as in causation, to the nitroid crises accompanying arsphenamine injections. The adrenals are overwhelmed with poisons.

AN ADRENAL FORM OF MALARIA

Fraga, a South American physician, reports three cases of severe malaria in which the syndrome of acute hypoadrenia was present and which he believes was undoubtedly the result of the malarial toxemia. He states that the clinical importance of this form of malaria lies in the fact that the adrenal principle will tide the patient past the danger point. In what he terms "the algid form" intravenous injections of adrenalin solution "may complete the triumph of the quinine;" but in the less severe cases opotherapy (gland feeding) alone may prove effectual.—Journal A. M. A., Oct. 26, 1918.

Remarks: The two foregoing items taken from the same abstract page "show which way the wind is blowing." To my mind hypoadrenia is present in every case of malaria, and is the cause of the severe asthenia which prostrates the patient after the chill. I mentioned this several years ago and quote from Chapter VII of my book "The Internal Secretions in Practical Medicine:" "I have put forward a theory regarding the adrenals in malaria which is yet to be discredited or proved. I believe that in one stage in the cycle of experiences in malaria there is a decided adrenal excitation, due to the sudden periodical liberation of the plasmodia and, of course, their toxins. One encounters the dry mouth as often as salivation, both manifestations of sympathetic stimulation. The heart action is always rapid and sometimes irregular. Then, as an aftermath of the chill, we find the muscular relaxation, prostration, depression and asthenia, all of which are identical with the findings of severe adrenal insufficiency."

If there is an effort made to forestall the expected adrenal "let down" by suitable organotherapy early, the severity of the weakness may be diminished and the possibility of such serious conditions as Fraga speaks of is minimized. This is exactly what is suggested repeatedly elsewhere, in influenza, alimentary toxemia, pneumonia, neurasthenia, etc. Render prophylactic adrenal support by suitable pluriglandular therapy, especially in individuals who show evidence of hypoadrenia to start with.

ADRENAL THERAPY IN MALARIA

Nicola Pende, Italy's leading endocrinologist and the author of the most comprehensive treatise on this subject, urges the routine consideration of the adrenal functions in malaria. In fact, he begins his treatment by support-

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ing adrenal function. He insists that a large share of the success of his method fully outlined in the article, is due to the early adrenal medication which "wards off the vaso-motor collapse" not merely from the quinine used but from the severe toxemia of the disease itself. (For it must be remembered that quinine is a poison just as are the protozoal toxins.)—Il Polyclinico, Nov. 4, 1917.

IODINE IDIOSYNCRASY AND THE ADRENALS

Clinical experience by G. Milian seems to have established the fact that iodism is but a phase of hypoadrenia! In a communication published in Paris Medical (May 5, 1917, p. 374) he tells of the prompt control of the symptoms of severe iodism in a patient taking an intensive course in KI by the administration of adrenalin. It is stated that the symptoms could be immediately dissipated by this treatment, or their appearance prevented by simultaneous adrenal medication. Quoting from his remarks: "The preventative and curative influence in iodism is important, not only because it permits us to push KI without fear, but also theoretically because it shows us that the iodine symptoms come from from adrenal insufficiency. Thus is overthrown still one more of the old 'idiosyncrasies.'"

Remarks: If the patient is subnormal in regard to adrenal function, and it must be remembered that syphilis is indeed a severe toxemia and one of the prime causes of structural disease of the glands of internal secretion, it is not difficult to find traces of the expected symptoms—hypotension, hypothermia, asthenia and malnutrition—and if a condition of adrenal insufficiency is diagnosed, adrenal feeding is distinctly in order, plus the associated specific treatment. Further it has been repeatedly shown that the severe reactions which may follow arsphenamine (salvarsan) injections are of adrenal origin and may be aborted by prompt adrenalin injections. In fact, these so-called "nitroid crises" are to be expected in the hypoadrenic individuals, and a preliminary course of adrenal feeding, or a simultaneous injection of 10 or 15 minims of adrenalin solution is being quite commonly used with arsphenamine as a prophylactic measure. Remember that the adrenal glands are extremely sensitive to poisons of all kinds, from within or from without, and both iodine and arsenic, in the doses ordinarily given in syphilis, are poisonous.

DYSPEPSIA OF ADRENAL ORIGIN

Prof. Maurice Loeper and his associates comment on certain gastro-intestinal disturbances which form part of the clinical picture of Addison's disease, and state that similar digestive disturbances are frequently encountered now in soldiers suffering from the strain of the war or convalescing from disease or infections or wounds. There is nothing characteristic about the digestive disturbances of these "incomplete adrenal states," as they call them, and we have no accurate clinical means of detecting this relative insufficiency on the part of the adrenals. They have made a practice for several months of administering to their patients with dyspeptic disturbances and obstinate constipation, small daily injections of from 0.1 to 1 mg. of adrenalin. Some were not affected by it in the least, but others were transformed by it. By the third injection the digestive discomfort disappeared, the stools became regular and assimilation more perfect, so that the men soon increased in weight. Along with this the blood pressure rose, the asthenia subsided and in one man with much pigmentation this also cleared up as the intestinal phenomena improved. The improvement under the adrenalin was in striking contrast to the lack of benefit from the usual measures applied to combat the dyspepsia. They explain the benefit by the tonic action of the adrenal principle on the nervous system, thus enabling it to modify some of the nervous reactions of the abdomen. An excess as well as a deficit of adrenin may generate abdominal trouble. We know that adrenin acts on the smooth muscle fibers of the vessels and bronchi, and probably the smooth muscle fibers of the stomach and bowel do not escape this influence. Hypoadrenia may influence the secretory activity of other abdominal glands, and the study of these adrenal dyspeptics seems to confirm this assumption. The difference between the gastric acidity after a test meal without and repeated with a preceding injection, of adrenalin shows an appreciable rise in the acidity under its influence. Radioscopy also shows a marked regulating influence on the motor functioning of the stomach and bowel. In six of the men in question the bismuth had scarcely reached the transverse colon by the seventh hour, but after a dose of adrenalin it was found in the rectum by the seventh hour, testifying to the acceleration of the passage of the bowel contents.—*Progres Medicale*, July 21, 1917.

Remarks: All of which goes to show how intimate the adrenals are with digestion. It also explains why

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"asthenics of the adrenal type" have so many abdominal difficulties; and why, when the adrenal functions are regulated, the digestive difficulties are favorably influenced with the increased vascular tone, metabolism and general muscular vigor. While Loeper's work was done with hypodermic injections of the adrenal principle, elsewhere in his writings on adrenal dysfunction, he speaks very highly of "total gland feeding" and recommends it as a rational measure in all asthenic states where the adrenals are implicated, or are likely to be.

"THE REAL NEURASTHENIA"

In a paper with the above title by Leonard Williams, of London, (The Practitioner, July 1917) there appear a number of most pertinent statements connecting "neurasthenia" with the ductless glands. The paper does not lend itself to abstracting; but several direct and unusual quotations are made:

"The real neurasthenia or shock is a circulatory matter."

"Graves's disease has been described as a chronic condition of fright, fight and flight—a good enough description if you will look beyond the bulging eyes and tremulous hands, to visualize the overactive adrenals, behaving chronically to produce the disease, as they behave suddenly in the presence of these emotions. Shock is an arterial matter and the adrenals hold intimate converse with the arteries."

"The proper circulation of the blood is second only in importance to its proper composition. Its composition is determined by the efficiency partly of the excretory organs, and partly by the ductless glands."

"In the true neurasthenia, a very wide divergence between the pulse rates in these two positions (standing and recumbent) is always present; and, what is worthy of note, is the fact that this is the only objective phenomenon which is present."

"When the bulb (medulla) is in watchful health this control (of the 'tone' of the vessels) is active and unerring. When it is out of health, things happen. One kind of toxemia may give rise to an undue pressor effect; another kind, to a depressor. These bio-chemical questions are functions of the endocrine system.

. . . If you hit the medulla in the face, or shake it, as a terrier shakes a rat, it falters. The contractile power is impaired, the vascular tone is lowered, the ves-

sels dilate, the blood-pressure falls, the various organs are insufficiently supplied, and there emerges the real neurasthenia; a tremulous, elusive, emaciating phantom, full of subjectivities"

"As to treatment—how is one to treat a battered bulb except by the sedative of a purified and well composed blood supply? The purification refers to drainage, and the good composition to the tribute of the endocrine glands. Of the former I will say nothing; it is so banal that few ever consider it! With regard to the latter, I permit myself to fling wide my restraint in a parting shot, and boldly call attention to the practical identity in the symptomatology of the real neurasthenia with that of adrenal insufficiency."

LOW URINARY SOLIDS AND ASTHENIA

The careful student of asthenic conditions and hypoadrenia cannot but remark how commonly the urinary solids are reduced both relatively and actually. The urea may be less than one per cent. and the total solids one half the average for a normal individual of similar weight. There is a reason for this defective elimination that lies outside of the renal and urinary field. The patient known to be suffering from hypocrinism is metabolically below par. His powers of oxidation are badly deranged and the normal wastes are not delivered to the liver for preparation there into urea and other products suitable for excretion by the kidneys.

Professor Slosse, of Brussels, has shown that the thyroid produces a "deaminizing hormone" the function of which is to activate the metabolism of protein wastes. In hypothyroidism low urea elimination is practically always present.

Recently Duval and Grigaut at the Allied Congress on the Biology of War (held in Paris, Oct. 19, 1918) gave figures to show that the nitrogen residues (estimated by blood chemistry) of the wounded and especially those who suffered from shock were much greater than normal, while, of course, the urea elimination was extremely low. According to them this deficient metabolism, a factor largely controlled by the endocrine glands, is the real basis for the "toxic accidents of shock."

At the same Congress, Claud Vincent made this statement: "The fighting man loses his tonus. . . He is an hypotensive."

In routine clinical work hypoadrenia is usually ac-

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accompanied by malelimination, as manifested by the low urea and total solids. The treatment MUST include measures calculated to stimulate metabolic activity, and especially those subtle chemical factors which not merely regulate the fitting together of the so-called "urea precursors," but the fundamental cellular chemistry.

It is of interest to note that suitable pluriglandular therapy many times has reestablished tone, not merely in so far as the patient's feelings are concerned, nor even by sphygmomanometry alone, but also by the beneficial change in the amount of wastes eliminated in the 24-hour urinary output.

PROGRESSIVE MUSCULAR ATROPHY AND THE ADRENALS

F. H. McCrudden, of Boston, (Archives of Internal Medicine, Feb. 1918) has gathered sufficient clinical and laboratory data to establish a relationship between adrenal dysfunction and progressive muscular atrophy. Without going fully into the details of his extensive studies, he reports that the severe musculo-asthenic condition pathognomonic of this disease is fundamentally due to hypoglycemia which, in turn, is the result of a defective glycogenesis, the ingested carbohydrates being changed into other elements than the glycogen necessary for the normal muscular nutrition. The cause of this has been pinned down to deranged adrenal functioning, and it is possible that as a result of this research work, there may be hope for those suffering from what has heretofore been supposed to be a hopeless disease. It is also of special interest in view of the great amount of work done by Sajous, Sergent, Loeper and others which has connected the less serious and functional (rather than organic) muscular dystrophies with adrenal dysfunction; and adds importance to our consideration of the adrenals as prime factors in the large class of neuro-musculo-dynamic disorders.

APPENDIX

OPPORTUNITY is taken here to make a brief statement about the "laboratory of applied endocrinology" located near Los Angeles, in Glendale, California, and directed by the writer and maintained by the good-will of many physicians throughout the country.

This institution is an outgrowth of efforts started nearly ten years ago, and its function is to foster and develop "practical endocrinology"—organotherapy—along lines which it is believed are sound. Briefly, the fundamental principle upon which this work is based is this: "Pluriglandular disorder is much more frequent than disorders involving a single gland of internal secretion; hence the reinforcement of an indicated organotherapy extract with one or more synergists many times radically alters the results for the better. In fact it may make the difference between success and failure."

Many experiments have been made to develop more useful glandular products, and an important branch of the work of this laboratory is the production for interested physicians of pluriglandular formulas after their own ideas. Scores of these "special formulas" have been made and used with advantage. Perhaps this phase of our work may be of interest to the reader, in which event a letter to the laboratory with your suggestions will be given personal attention.

To maintain the laboratory a number of stock formulas are sold either direct to physicians or on prescription. Further information about these combinations is found in the comprehensive booklet "Pluriglandular Therapy," which will be sent on request.

NO. 1. CAPS. ADRENO-SPERMIN COMP.

Dynamogenic.

Adrenal Gland (total) gr. $\frac{1}{4}$
Thyroid Gland (U. S. P.) gr. 1-12
Spermin Extr. (from Gonads)
Brain and Spinal Cord 2a gr. 1
Calc. Glycerophosphate q. s. ad gr. 3

A neuro-muscular stimulant acting thru the endocrine glands. Indicated in conditions where general cell stimulation is desired, e. g., as an adjuvant in many chronic disorders; deficient oxidation with low urinary solids; the fatigue syndrome and rundown conditions; circulatory inefficiency with hypotension; many functional neuroses including neurasthenia, etc.; sensitivity, etc.

Dose: One capsule 3 or 4 times a day before meals and on retiring.

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Caps. Adreno-Spermin Co. is a successful attempt to fit together the dynamogenic principles of the gonads (spermin), adrenals (adrenin) and brain (lecithin) with a small dose of thyroid. In the numerous phases of insufficient cellular activity or metabolic laziness, these endocrine principles are Nature's own stimulants. As a profitable excipient in place of the usual milk sugar, the glycerophosphate of calcium is used, thus adding the well-known neuro-tonic effect of this salt.

NO. 2. CAPS. ANTERO-PITUITARY COMP.

Morphogenic.

Anterior Pituitary Body gr. 2
Thymus Gland gr. 1
Thyroid Gland (U. S. P.) gr. 1-12
Calcium-phosphorus Comp.* q. s. ad gr. 5

A growth stimulant and endocrine regulator. Indicated in deficient morphological development — "hypoplasia" — in childhood and youth; as an adjuvant to thyroid feeding in cretinism; in mongolism and other endocrine dyscrasias in children.

Dose: Two capsules twice a day.

This formula embodies an attempt to increase the results of the "gland feeding," now considered the ideal measure in developmental disorders in children. The active principle of the glandular anterior part of the pituitary body is probably the most effective remedy at present known. The small amount of thyroid renders the combination more active and where the thyroid element in a given case is quite prominent, as in cretinism, one can add more thyroid.

NO. 3. CAPS. PLACENTO-MAMMARY COMP.

Galactogenic.

Decalcified Placenta gr. 2
Mammary Substance gr. 1½
Pituitary Body (total) gr. 1-3
Calcium-phosphorus Comp. q. s. ad. gr. 5

A post-partum stimulant, to increase the production of milk; to prevent agalactia as well as to increase a faulty supply; and to facilitate uterine involution.

Dose: One capsule at each meal. Often best to give two capsules for 8 or 10 days.

Much study in the past four years has demonstrated the real galactogenic value of placenta. Mammary gland has a similar and more easily understood action due to the principle of homostimulation. It also is a pelvic depletant and this action cooperates with the musculo-tonic influence now generally accredited to the pituitary principles. When prescribed as a prophylactic, rather

than as a last hope that the milk may be increased, one gets better results.

NO. 4. CAPS. THYRO-OVARIAN COMP.

Ovarian Substance } gr. 2½
Dose. Corpora Lutea }
Thyroid Gland (U. S. P.) gr. 1-12
Pituitary Gland (total) gr. ¼
Calcium-phosphorus Comp. q. s. ad. gr. 8

An ovaro-uterine remedy. Indicated in amenorrhea and hypo-ovarism; numerous neuroses of pelvic origin; menstrual and climacteric disorders; circulatory imbalance of ovarian origin; etc.

Dose: One capsule at each meal. (May be doubled five days before, and omitted during and for some days following the menses.)

Ovarian organotherapy has attained an important position in gynecology, due to its efficacy. No procedure or remedy can begin to take the place of ovarian organotherapy where the noteworthy stimulant and regulative influence upon ovarian function is needed.

Dalche, of Paris, and Hertoghe, of Antwerp, were the first to emphasize the remarkable synergism between the thyroid and ovaries; and for years the former has been successfully using combinations of these glands in preference to either alone.

Where ovarian or luteal therapy is indicated—in amenorrhea, dysmenorrhea, neurasthenia, the climacteric, etc.—this combination is valuable because of the augmented hormone action that it facilitates.

A comprehensive brochure entitled "Ovarian Dysunction" goes into the subject more fully, and will be sent to any interested physician.

NO. 5. CAPS. HEPATO-SPLENIC CO.

Trophogenic.

Liver Parenchyma
Spleen Substance 22 gr. 2
Powd. Bile Salts gr. 1½
Adrene-Spermin Co. (No. 1) gr. 1

A nutrition stimulant. Indicated in hepato-biliary insufficiency; malnutrition in malaria, tuberculosis, etc.; alimentary toxemia; intestinal stasis, and to favor an increase in weight.

Dose: One or two capsules at meals.

A good deal has been said in favor of splenic organotherapy in various nutritional disorders. Its value has been reiterated many times. Evidently its increasing use means that its results are worth while; and Bayle explains its value by attributing a mineral saving or colloidogenic influence to the splenic active principle. Besides stimulat-

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ing the liver and bile production this combination is a trophogenic stimulant in hepatic insufficiency and cirrhosis, ptosis, tuberculosis, chronic malaria, etc.

NO. 6. CAPS. PANCREAS COMP.

Hyperthyroidism.

Adrenal Gland
Pituitary Gland (total) an gr. $\frac{1}{2}$
Ovarian Substance gr. 1
Pancreas Substance q. s. ad gr. 5

A sympathetic sedative. Indicated in the cardiac and nervous disorders of increased endocrine action, as in hyperthyroidism.

Dose: One capsule, 3 to 6 times a day, between meals.

Various observers have remarked that benefit follows the administration of pancreas in sympathetic irritability, and in no endocrine disorder is this symptom-complex so marked as in hyperthyroidism.

Adrenal substance also has been used in hyperthyroidism for its symptomatic value which is probably due to its cardio-tonic effect. Pituitary is added for the same reason and because its effect on unstriped muscle is just the kind of steadyng needed in the cellular excitement of Graves's disease and allied disorders.

In hyperthyroidism eliminate sources of toxemia (teeth, tonsils, sinuses, bowels, gall-bladder, colon, etc.), neutralize with generous doses of Calcium Phosphorus Co. (See No. 11) and try this combination.

NOS. 7-9. CAPS THYROID COMP. GR. $\frac{1}{8}$ - $\frac{1}{4}$ - $\frac{1}{2}$

Dose. Thyroid Gland (U. S. P.) gr. $\frac{1}{8}$
Calcium-Phosphorus Comp. q. s. ad. gr. 5

Indicated in the developmental and nutritional dyscrasias attributed to defective thyroid functioning; and, generally, where thyroid stimulation is desirable.

Dose: From $\frac{1}{8}$ to $\frac{1}{2}$ a grain t.i.d.

Every case of subthyroidism, whether of the usually overlooked minor form, or the well differentiated hypothyroidism, functional or organic, is in a state of metabolic insufficiency. This is why thyroid is given—to stimulate metabolism.

Metabolic insufficiency means mineral starvation, for the increased wastes rob the body of its saline elements (principally alkalies) and cause acidosis. This is one reason why hypothyroidism is often accompanied by low urinary solids, also why adiposity is comparatively common.

Caps. Thyroid Comp. is an excellent, standardized thyroid product with a really useful excipient—a balanced alkaline-saline combination similar to the salts in the blood—instead of starch or milk sugar.

NO. 10. THYROID TESTING CAPSULES

A means of measuring thyroid secretory function and thereby differentiating simple goiter from early or suppressed thyroidism.

Each package contains 3 boxes of 12 graduated capsules with instructions and charts.

It is possible to secure valuable information as to the functional capacity of a thyroid gland, whether enlarged or not. The administration of step-ladder doses of thyroid extract in a routine, uniform manner, causes changes which can be recorded and which serve as a useful "therapeutic test."

The treatment of simple goiter is quite the opposite of that given for thyroidism and it is far better (and more scientific) to ascertain something of the thyroid function in a given case than to learn it from our failures. This is a test worthy of use in every case where there is any doubt as to the apathy or undue sensitiveness of the thyroid.

NO. 11. TABS. CALCIUM PHOSPHORUS COMP.

Remineralization.

Each 100 parts contains:
 Magnesium Phosphate Gm. 2
 Calcium Phosphate (dibasic)
 Calcium Glycophosphate ss Gm. 8
 Potassium Bicarbonate Gm. 32
 Sodium Bicarbonate Gm. 50

An alkaline "mineral food" for the neutralization of acidosis and the re-establishment of the mineral reserve of the organism. A rational adjurant in toxemias and especially in chronic "demineralization" associated with endocrine deficiencies.

Dose: Four to six grams a day, in 2 or 3 doses, crushed and swallowed with much water (2 glasses best) remote from meals.

From the start the excipient in this laboratory has been "the mineral salts similar in proportion to those in the blood." The above formula is identical save that the sodium chloride is omitted. Under the heading "Caps. Thyroid Comp." the philosophy of this alkaline-saline combination is outlined. To satisfy a number of enthusiastic users the "salts" are now obtainable in tablet form, so that as generous a dosage can be given as may seem advisable. This is indeed an excellent associate remedy in many chronic disorders where the toxemia has seriously reduced the organism's reserve of alkalies.

NO. 12. CAPS. AMYLO-TRYPSIN COMP.

Digestant.

*Amylopsin (Diastase) gr. $\frac{1}{2}$
 Pancreatin (U. S. P. IX) gr. $2\frac{1}{2}$
 Papain ("Vegetable Papain") gr. $\frac{1}{2}$
 Berberine Sulphate gr. 1-12
 Carminatives (Cinnamon, etc.) q. s.*

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A polypenzyme digestant formula, acting in the stomach and upper intestine. Indicated in hypopepsia and indigestion generally.

Dose: One to three capsules, preferably 2 or 3 hours after meals.

The above enzyme formula "speaks for itself." It contains nothing superfluous or incompatible. The ferments are of well-tried efficacy and serve to increase digestion in both stomach and intestines. The added berberine augments the mucosal carminative effects. An unusually efficient digestant preparation.

NO. 13. CAPS. HEMOGLOBIN COMP.

Hematinic.

Repar. Hemoglobin gr. 4

Dose. Spleen Parenchyma gr. 1

Ac. Nuclein (Nuclein) gr. 1/2

Calcium Phosphorus Co. q. s. ad gr. 8

Absorbable and utilizable "organic iron" reinforced with the hemopoietic principle from the spleen and the well-known leuko-cyto-stimulant, nuclein. A rational remedy for anemia and allied nutritional disorders.

Dose: One capsule, 3 to 6 times a day.

Hemoglobin is quite the best form of iron for internal administration. It seems to serve better than any other more commonly used hematinic. The combination with spleen and nuclein is indeed a happy one. The former is said to encourage blood formation and "the fixation of iron" (Ascher) while nuclein is a well known and remarkable stimulant of white cell formation and has been recommended for years for its "resistance stimulating" effects.

The foregoing combinations are worthy of your confidence. The ingredients are carefully processed. The formulas are not secret. There are no trade names and no indications on the labels or in the packages. In other words, every possible effort is made to conserve the well-established fundamentals of ethical pharmacy and medicine. Further information about these stock formulas, or about a number of special formulas which are also obtainable, may be secured from the undersigned, who will be pleased to enter into correspondence with any interested physician, and to send, gratis, The Organotherapy Review each month to those who desire it.

From the Laboratory of
HENRY R. HARROWER. M. D.
Glendale, California

I INTRODUCTORY REMARKS

WITH apologies to my readers I wish to preface this brochure with a few explanatory remarks.

After a number of years of study of the internal secretions, much travelling in near a dozen countries to visit workers especially interested in various phases of this fascinating subject, a fairly careful study of the endocrine literature (resulting in three books and a number of articles on internal secretory subjects), and not a little "puttering" in an inadequate laboratory, I have established a "laboratory of applied endocrinology" where I hope to develop a number of ideas which I believe will broaden the practical value of organotherapy.

In considering how to put this laboratory on a satisfactory and self-supporting basis, I decided in favor of building a business with certain organotherapeutic products in order that the profit derived from their sale might maintain the institution and that, as it grows, opportunities might be afforded to develop the suggestions of colleagues who, like myself, have had more or less intangible ideas which have been difficult or impossible of materialization because of limited finances or facilities.

Having made this decision, the most natural way to start seemed to be to prepare a number of pluriglandular formulas which I had been in the habit of prescribing or recommending to my medical friends, and ask these friends to use them if they appeared reasonable. These formulas are given and their therapeutic possibilities are briefly discussed in the following pages, and your favorable consideration of them is solicited.

The next development of the work of this laboratory was the production from time to time of small experimental quantities of various organotherapeutic preparations for colleagues; and already this phase of our work bids fair to accomplish much in the way of broadening organotherapy. Indeed this was the underlying reason for deciding to begin operations. Such "Special Formulas" as may be requested from day to day are worked out with or without my own suggestions. These formu-

las are made in smaller quantities than manufacturing pharmacists care to consider—only 300 suffices for a minimum batch, and I have occasionally made still less—and are modified from time to time as it seems advisable. Thus useful combinations are developed and it is a source of great encouragement to me to be able also to submit here a number of these "S. F.'s" with suggestive clinical indications and other data.

Arrangements have been made for the distribution of the stock preparations in many centers. This will be extended in due time and whenever a physician wishes my pluriglandular formulas stocked for his convenience in prescribing, this will be taken care of. For the time being the "special formulas" cannot be secured thru the trade, though they will be supplied direct (and usually made specially) on order by physicians or to their prescription pharmacists. They are not sold to wholesalers.

Since the first editions of this brochure have been in print much encouraging correspondence has come to my desk. From one letter I quote a very happy statement: "I have been indebted to you for putting me on to a number of good things in your two books, and now that I am using your own preparations I am getting better results than ever. There is no doubt that your idea about combining glands is right. . . ."

This opportunity is taken to welcome correspondence and the chance to co-operate with the profession in any manner. A little periodical, THE ORGANOTHERAPEUTIC REVIEW, is published by me with the object of keeping interested friends in touch with what is going on in the laboratory, and also with the essentials of the progress in organotherapy. It has been very well spoken of and will be sent from month to month with my compliments to those physicians who request it.

Glendale, California.
October, 1918.

Henry R. Harrower.

II

"THE PLURIGLANDULAR THEORY"

A FUNDAMENTAL principle which has broadened organotherapy in a most remarkable way is embodied in the following statement: "Pluriglandular disorder is much more frequent than disorders involving a single gland of internal secretion; hence the reinforcement of an indicated organotherapeutic extract with one or more synergists many times radically alters the results for the better. In fact it may make the difference between success and failure."

It is not difficult to understand that a general influence for harm, toxic, nutritional or emotional, hardly can be expected to limit its effects to a single small part of the organism. A severe toxemia such as we find in pneumonia, typhoid, intestinal stasis or poisoning with alcohol, morphin or other drugs, deranges the function of the body as a whole although in one instance a certain part of it, say the liver, may be more obviously disordered than in another. This applies equally to the endocrine glands and the writer frequently has said with emphasis that "there never was a uniglandular endocrine disorder!" This may seem to be a rather inclusive statement; but it would be difficult to convince me of the reverse, for once one has learned the underlying principle of hormone action and the extreme intimacy of the endocrine glands and their close dependence the one upon the other, it is not easy to conceive of any obvious or hidden disease process affecting only one or two of these remarkable little organs. They may be remotely situated from one another, but they are very closely bound together by hormone ties.

Clinical Endocrine Relationships

The subject is so important and the clinical and therapeutic deductions are so valuable that it may be well to give some more study to this "theory." Take as an example a fairly common ductless glandular disorder—hypothyroidism. It is seen in all gradations and its own direct manifestations are always intertwined with those

of other origin. No case of myxedema or cretinism, or even of the less marked but more important minor thyroid insufficiency, shows the manifestations of thyroid dysfunction alone. Metabolism as a whole is reduced—and the thyroid is not the only endocrine gland concerned in the regulation of metabolism. Gonad function is disturbed, and in cretins it practically never develops at all. Then, too, thyroid disorder is so very commonly associated with menstrual function that the gynecologist these days never considers a case of menstrual derangement without considering the thyroid function with that of the ovaries. The sympathetic system, which we have every reason to believe is controlled by the hormones produced in the chromaffin tissue of the adrenal glands, is very decidedly affected in hypothyroidism, and in the well marked cases the blood pressure is low, circulation is very much below par, and the usual sympathetic reactions are dulled or even lost.

Again the so-called "compensatory hypertrophy" of some glands during functional or organic insufficiency of some other intimately associated gland of internal secretion adds to the impression that these organs must be considered together rather than separately. The cycle of the development and atrophy of the mammary glands in relation to the variations of ovarian function is one instance; the not infrequent enlargement of the thyroid (and more rarely the pituitary) during the period of normal ovarian inactivity—during gestation and at the beginning of the menopause; possibly the interstitial glandular hypertrophy of the prostate when the testes are in process of normal atrophy; and other physiological functional dependencies which we do not need to mention, all tend to the conviction that we must no longer consider endocrine disease, functional or organic, as involving the gland or glands alone which most obviously are affected.

Synergistic Organotherapy

This being the case we should be able to make good use of this principle in our work, both diagnostic and organotherapeutic; and the added information that we acquire by viewing various symptoms-complex from the "pluriglandular viewpoint" are just as encouraging as

the better results that we get from pluriglandular as compared with uniglandular endocrine preparations.

In brief, then, the facts warrant the combination of synergistic gland extracts no matter whether we can see clear clinical evidence of disorder of these synergistic glands. It must be remembered that symptoms do not manifest themselves for quite some time after the beginnings of actual dysfunction in the cells. The ovarian side of goiter, or the thyroid side of dysovarism does not necessarily accompany the first evidence of disturbed secretion in the gland originally affected.

Nor must we limit our new viewpoint to pairs of organs like the thyroid and the gonads just referred to. In hyperthyroidism, for example, not only may we find deranged ovarian function; but I am confident that not a few of the symptoms of sympathetic irritability are not so much due to the excess of thyroid stuff itself as to the undue stimulation by it of the adrenal glands. Really then what we call hyperthyroidism often is hyperadrenia! Or hypercrinism—a generally increased endocrine activity due to a condition which has increased thyroid secretion beyond all reasonable bounds and consequently simultaneously has stimulated the pituitary, adrenals, gonads and other endocrine glands. If this is the case, medication to be successful should take the whole endocrine system into consideration and not the offending thyroid alone. The same applies even more to conditions of hypocrinism which result from pluriglandular insufficiency.

Combinations Superior to Single Extracts

This explains why combinations of various endocrine preparations so often excel single extracts. In previous communications, and in both of my books referred to elsewhere, I have strongly urged the combination of suited products of this kind. The profession is thoroughly converted to moderate polypharmacy, and we combine our A. B. & S., or our I. Q. & S., our mercury and potassium iodide, or many other well-known pharmaceutical products. Rarely is a prescription written for a single remedy, for we are absolutely convinced that synergism is possible in pharmacology just as it is in physiology. Should there, then, be any real basis for

criticism of pluriglandular therapy by those who routinely apply the same principles in polypharmacy, especially when we recall that the blood itself contains in solution a host of differing chemical substances, some synergistic and some antagonistic?

As a matter of fact such portions of a pluriglandular mixture given per os as are absorbed into the blood, merely amplify the sum total of hormones circulating in the blood and according to the principle of homostimulation outlined in the body of this book, arouse into increased functional action those organs whose work it is to produce hormones similar to those which have been administered. Thus hypocrinism is reduced and the aggregate of hormone stimuli is increased.

Hormone "Hunger" and "Fullness"

The intricacies of cell chemistry or of the chemistry of the plasma can only be surmised. Even the physiologists have not been able to ascertain much of this information. Like us they presume and deduce. In my opinion, and it is shared by many others, when we augment the hormone content of the blood by means of pluriglandular therapy, the effect most prominent is the effect most needed, for it is not unreasonable to suppose that in the subtle changes involved in the selection from the blood by certain cell-aggregates of a certain special substance, there is a condition of "hunger" or "satiety" for the necessary hormone, and that when this hypothetical "hunger" for a certain hormone is greater than usual, the capacity to select and utilize the artificially supplemented amounts of that substance (organotherapy) is correspondingly greater. Presumably also the reverse is equally true. So when we give, let us say, a thyroid-ovary-pituitary combination, as we very often do, the thyroid benefit is greatest when the thyroid insufficiency is most and the ovarian reaction is most when the need for the ovarian principles predominates, and so forth.

All this is hypothesis. We can not prove it. We can only note that in one case the effects of a pluriglandular combination lean to those expected from one of the glands presumed to be involved, and in another case identical therapy has a different result. This is similar

in principle to the statements made elsewhere in regard to the differing reactions in various individuals to whom the same form of organotherapy is given. In one case the results are more striking than in another, undoubtedly because the receptivity of the cells to hormone stimuli differs from the corresponding cells of others, either because the need for these stimuli is less, the hypothetical "hunger" for the hormone is decreased, or the capacity to avail themselves of the offered hormonic assistance is less.

Despite the lack of "positive information," which I have long since given up worrying about (and thereby depriving myself and my patients of benefit), and the undoubted need for more accurate data, we believe from many most encouraging clinical experiences that pluriglandular disorder is the rule and, therefore, that pluriglandular therapy is the logical corollary.

III

EFFECTIVE ORGANOTHERAPEUTIC FORMULAS

WITH the foregoing "theory" in process of metamorphosis in our minds into a "principle," we begin to see in a different light many things which have confronted us in the past. Indeed when one grasps this fundamental proposition, it is surprising how many times our diagnostics are broadened and our opportunities for therapeutic service are enlarged. The endocrine side of chronic disease takes on added interest and we are easily convinced that hypocrinism must complicate many long-standing ailments.

If the nutrition of the body is reduced, so is the nutrition of the glands of internal secretion and their capacity to produce their hormones is also reduced, with the production of a vicious circle. To stimulate these glands at the same time that all the other means of encouraging nutrition are being used, is both a rational and resultful procedure.

If the disorder under consideration is accompanied by toxemia, how can the increased quantities of toxins circulating in the blood not affect the endocrine glands which are particularly susceptible to toxic influences and, in a large degree, are supposed to assist in destroying noxious substances? (The thyroid, parathyroids, liver and, possibly, the adrenals have a well-demonstrated toxin-destroying faculty, and long-continued toxemia can not but "wear out" the organs thus overburdened.) And how many and varied are the diseases in which toxemia is prominent? To attempt to rehabilitate the endocrine glands by means of organotherapy is quite in order, if at the same time a thorough-going effort is made to eliminate the cause. Why give any kind of treatment in hypoadrenia if the cause is overlooked? This is as bad as removing an unruly thyroid and leaving the toxic or infective cause to "knock out" the thyroid remainder which the surgeon is forced to leave.

Several fundamental forms of pluriglandular therapy are represented by a series of stock formulas made under

my supervision. They represent a well-considered attempt to apply the principles of endocrinology to certain fairly large groups of cases. In other instances other formulas are advised and they can be found in Chapter VI. Where necessary, stock formulas can be modified by the addition or subtraction of any ingredients.

A Remedy for Hypocrinism

When an individual has suffered from any long-continued irritation of the endocrine glands, they will begin to fall down in their service to the body. As we have seen toxic, emotional and nutritional influences wear out the endocrine glands as well as the rest of the cells of the body, and since the hormones (Greek, I arouse or set in motion) "drive" the bodily machine they are unusually essential to health. Hence augmented hormone production is particularly helpful in the treatment of all "run-down conditions," whether due to disease or to the normal asthenia of age.

With evidence that we have to deal with hypocrinism —easy fatigue, asthenias of all varieties (myasthenia, neurasthenia, psychasthenia, etc.), poor circulation and low blood pressure and faulty oxidation and elimination —hormonic treatment is in order and I have seen splendid results accrue from a pluriglandular stimulant which I have called Caps. Adreno-Spermin Comp.* The formula is as follows:

No. 1

Caps. Adreno-Spermin Co.

Desic. Adrenal Gld. (total) gr. $\frac{1}{4}$
Thyroid Gld. (U. S. P. IX) gr. 1-12
Spermin Extr. (from Gonads)
Brain and Sp. Cord aa gr. 1
Calc. Glycerophos. q. s. gr. 5

This formula is intended to antagonize "endocrine apathy" and to augment the work of the so-called "adrenal system." It gently encourages the work of those

*Attention is called to the fact that no trade names are used in connection with any products of my laboratory; that the formulas are open to the profession; that no indications appear on the label and no explanatory literature accompanies the package; and, to my way of thinking, no unwarranted therapeutic claims are made. Every attempt is made to adhere closely to the fundamental principles of ethics both as regards medicine and pharmacy.—H. R. H.

endocrine glands responsible for the dynamogenic functions of the organism and is recommended as a neuro-musculo-circulatory stimulant in asthenic, run-down states. The contained adrenin favors increased adrenal efficiency and is responsible in part for the increase in blood pressure which usually follows its administration for some weeks. Its pressor action is quite unlike that due to the drugs usually administered for this purpose, and the upward curve in the blood pressure chart is the result of enhanced endocrine efficiency.

A good deal has been written about the effects of spermin as a stimulant of cell oxidation. Too many claims have been made, to my mind; but unquestionably spermin is a cell stimulant and the more crude testicular substance alone will increase vigor and cellular tone in both sexes. At least it is a useful addition to this formula as many tests of different "cell tonic formulas" have proved. Briefly, spermin, orchic substance or the "liquide testiculaire" originally used by Brown-Sequard on himself in his laboratory in Paris in 1879, exerts a myostimulant, invigorating effect (definitely measurable by means of Mosso's ergograph) as well as its well-known homostimulant effect. Its addition to the Adreno-Spermin formula favors this salutary dynamogenic effect.

It should not be necessary to dwell upon the therapeutic value of lecithin. It is organic phosphorus and more of a cell-nutrient than a cell stimulant. The same is true of calcium glycerophosphate (which, by the way, originally was discovered as a product of the gonads by a French investigator and there seems to be no doubt that appreciable amounts of glycerophosphoric acid can be secured from testicular substance as well as from semen). The calcium glycerophosphate is used in place of the usual pharmaceutical excipient, sugar of milk, and has the added advantage of being a recognized "nutritive salt."

Finally there is included in this formula a small dose of U. S. P. thyroid gland. It is there for a very definite purpose. Such doses have a distinctly invigorating effect, especially in elderly individuals and in patients who are run-down as the result of fevers, toxemia and chronic disease generally. It is rarely enough to exert a real

"thyroid effect," but more than once I have compared the small dose of thyroid in a pluriglandular formula to the Worcestershire Sauce we are in the habit of using with our food—it seems to "bring out the flavor," and it makes a decided difference to the combination.

Altogether I am quite enthusiastic over this combination. Its action is so valuable as an adjuvant in many long-standing disorders and it is usually quite decidedly appreciable by the patient within a few weeks, and, to a certain extent, measurable by the physician through his sphygmometric records and also the elimination of urinary solids, that it does not have to be given "by faith" for very long. Of course the therapeutic response to three or four doses of Caps. Adreno-Spermin Comp. a day (preferably before meals) varies with the cellular and endocrine reactivity of the individual and also with what is done for them simultaneously. Many personal experiences and reports from numerous physicians have come in which increase my confidence in this excellent organotherapy tonic and reconstructant.

A Developmental Stimulant for Children

It has been shown that defective children always have a very important endocrine phase to their pathology. The subject of "children requiring special attention" is too large to be more than mentioned here in passing; but I think that it is fair to say that the unanimous opinion of the profession includes the ductless glands as prominent in the etiology of these difficult cases. There are many kinds of defective children other than the well-differentiated cretins, and practically all of them have a more or less well-pronounced hypothyroidism. Rarely is this unaccompanied by other endocrine derangements, and the same may be said of the "pure cretin"—his thyroid trouble may be altogether outspoken and frank, but he also has a pluriglandular disorder due to the lack of the stimuli the other glands of internal secretion ordinarily get from the thyroid.

This is really the reason for many failures with thyroid therapy in these cases. The associated endocrine disorders are not treated. Hence not merely in pluriglandular insufficiency in children, but in frank athyroid-

ism or a clear case of Froehlich's disease or hypopituitarism, the obviously indicated gland feeding is profitably supplemented by other extracts. This is particularly true of the thyroid and pituitary glands, and where the one is indicated the other may be added with benefit.

The essential part of the pituitary gland, the anterior lobe or true glandular portion, contains a principle isolated by Brailsford Robertson and named by him "tethelin." This hormone exerts a growth-stimulating effect in addition to its homostimulant effect upon the pituitary itself. It is used in backward children of the "indefinite" type, in pituitary insufficiency, in cretinism and for its purely morphogenic effect in dwarfism or achondroplasia.

Therefore I have used and recommended for years a combination for cases of this type and have seen some indubitable results, such as added intelligence of a type that could be measured by our present standards, the automatic descent of the testes in cryptorchidism, the development of a capacity to enunciate words and combine them into short sentences where previously this long-delayed power was impossible, the removal of chronic constipation lasting from birth and of years standing (when no other drugs were used simultaneously), and a modification of the malnutrition and especially the asthenia so often found in hypoplastic children. The basis of this formula has been modified and modified again and since the establishment of this laboratory the resultant combination has been called Caps. Antero-Pituitary Comp. with a formula like this:

No. 2

Caps. Antero-Pituitary Co.

Pituitary (Anterior Lobe) gr. 2

Desic. Thymus Gld. gr. 1

Thyroid Gld. (U. S. P. IX) gr. 1-12

Calcium Phosphorus Co. q. s. ad gr. 5

The addition of thymus is quite empirical. Several communications in the literature record benefit from this form of organotherapy in developmental defects in children and the only reasonable explanation of its possible value is in connection with its capacity to facilitate the metabolism of calcium salts which is supposed to be influenced by this gland and very often is defective in such cases. For the same reason my excipient, called

"Calcium Phosphorus Co.," is used. The formula of this combination of mineral salts will be found elsewhere (see Chapter IV) and the philosophy of its use is merely the principle of "remineralization" so well worked out by the French.

This formula, then, is intended to supplement the dietetic, hygienic and educational development of defective children and must be given for a number of months if any benefit is to be obtained.

My usual recommendations are something like this: "It is clear that we have a serious glandular derangement here. We seem to have had enough results from gland feeding in the past to warrant our using it at least until it has been proved useless. This takes from six months to a year. If you will give the child these gland extracts (explaining, if you will, some of the philosophy of the method and thus increasing the parent's confidence and future co-operation) for three or four months and there is enough accomplished to offer prospect of further benefit we will continue the treatment for six months or more, or until we are sure that it is doing no more good. The results may be seen before three months, they may not be seen till after six months, if no benefit occurs by that time we confess that this particular form of gland feeding is a failure and try again and at the end of a fruitless year we confess total failure, but not before this. It is a long job to re-educate these disordered gland functions." And the patient's parents agree that this is reasonable; and, indeed, it is the only thing to do and fortunately quite often it works.

The dose usually recommended is two capsules a day for 3 out of every 4 weeks for several months.

An Organotherapy Galactogogue

The habits of many wild and domestic animals of devouring the placenta suggests that perhaps Nature prompts these beasts to do this for a definite reason. Many years ago crude experiments were made to determine whether the placenta exerted a galactogogue effect and it was concluded that it does. More recently, since better preparations have been obtainable, the subject has been given careful clinical trial and it has been estab-

lished by tests in many cases that the production of milk is distinctly enhanced following the administration for some days of this somewhat strange remedy. Not only is the amount of milk increased but its quality is changed for the better, especially the fat content.

It has also been shown that placental opotherapy exerts an antagonistic action upon pelvic congestion and uterine subinvolution. It may be possibly this very feature that is Nature's reason for the habit of animals just referred to. Suffice it to say that in therapeutics this method is definitely useful not merely to prevent agalactia but as a prophylactic measure given early enough to augment a waning supply of milk.

On the principle of the synergistic action of organo-therapeutic preparations two important additions may be made to desiccated placenta—mammary substance and total pituitary substance. The former exerts its well-known homostimulant effect and at the same time also has an anti-ovarian effect, for the hormones of the mammae and ovaries counteract one another (this is the basis of the use of mammary extract in hyperovarism, conditions of unusual pelvic congestion and menorrhagia), and this is of additional advantage in postpartum conditions. The latter is given for the musculo-stimulant effect attributed to the pituitary principle, and this triad is an efficacious galactagogue combination:

No. 3

Caps. Placento-Mammary Co.

Desic. Placenta gr. 2

Mammary Substance gr. 1 $\frac{1}{2}$

Pituitary Gld. (total) gr. 1-3

Calcium Phosphorus Co. q. s. ad gr. 5

This preparation has been used successfully when there has been a serious reduction of the amount of milk secreted; but it is more rational as a prophylactic and is recommended as a routine procedure following labor. The initial dose is one or, preferably, two capsules at each of three meals daily for ten days or two weeks, thereafter continuing the administration of one capsule three times a day for several weeks.

Functional Ovarian Disorders

There is a large and increasing literature on the importance of augmenting or regulating the ovarian endo-

crine function by means of corpus luteum or total ovarian organotherapy. This is one of the "accepted" forms of organotherapy, for unfortunately some physicians still seem to believe that "there is not much in this organotherapy—except perhaps thyroid." Peculiarly enough this very statement has been made to me a number of times and I have had to smile, hence the added phrase about thyroid! Physicians who are not very "strong" on organotherapy always use thyroid in myxedema, they admit that adrenalin is an indispensable remedy and that it comes from an animal gland, and most of them have been convinced of the amazing effects of the posterior pituitary solution. The same is beginning to be true about corpus luteum and before long these same skeptics will have accepted the whole principle rather than the few most obvious parts of it.

At all events functional pelvic disorders and the reflex disturbances resulting therefrom for fifteen years or more have been successfully treated with suitable organotherapy, usually corpus luteum or ovary alone, and no method or drug can begin to take the place of such preparations, especially in a functional hypo-ovarism due to disturbed regulation of the ovarian hormone production, and to mitigate the numerous sympathetic-circulatory manifestations of the menopause, normal or artificial, pathological or physiological.

I can not begin to enumerate the emphatic opinions in favor of this measure; but wish to show that the use of corpus luteum or ovary alone is not likely to be so completely beneficial because the hormone-complex as a whole has not been taken into consideration. It has been shown by many investigators that the thyroid function is extraordinarily intimate with that of the ovaries. We know that goiter is often connected in some way with menstrual disorders, that pituitary insufficiency means gonad insufficiency, and so forth. Clinically we have found out that the thyroid and pituitary principles are synergists of the ovarian hormones and many times thyroid or pituitary feeding alone has benefited symptoms seemingly due to ovarian dysfunction. The combination of these gland products with ovarian substance is indeed useful, and it "hits the mark" more often than the single

extract for the very same reason that pluriglandular therapy in general excels the use of single extracts.

For years it has been the custom in France to use thyroid gland whenever ovarian feeding was indicated. The combination is superior to either of the single remedies. Dalche, of Paris, has explained this quite fully and clinical experience by hundreds of physicians has demonstrated that this idea is well founded. So I offer for your consideration this formula:

No. 4

Caps. Thyro-Ovarian Co.

Desic. Corpora Lutea { gr. 2½
Ovarian Substance |
Thyroid Gld. (U. S. P. IX) gr. 1-12
Pituitary Gld. (total) gr. ½
Calcium Phosphorus Co. q. s. ad gr. 5

The indications are virtually those of corpus luteum or total ovary substance as stated in numerous contributions to the literature of the past 8 or 10 years. The only contraindication is hyperthyroidism, for which I offer another formula on page 23 (Caps. Pancreas Comp.). This thyro-ovarian combination contains both the desiccated corpus luteum of pregnant animals and total ovarian extract and is indicated in dysovovarism with menstrual or climacteric disorders, nervous or circulatory. It is warmly recommended in the treatment (not necessarily as the whole treatment) of functional pelvic derangements such as amenorrhea, postponed menstruation, dysmenorrhea and the numerous symptoms due to circulatory imbalance of pelvic origin. Particularly does this combination excel corpus luteum alone in the control of the hormonic chaos which occasionally accompanies the menopause. Here the more or less sudden loss of a hormone stimulus to which the body has been accustomed for thirty years or more, causes very severe symptoms and among these are certainly some due to hypothyroidism resulting from the reduced stimuli to this gland. Small doses of thyroid are sometimes remarkably beneficial at the menopause for the very good reason just mentioned. The same is true of the pituitary extract largely because it antagonizes the general muscular atonicity (including that of the uterus and other pelvic structures) so usual at this period.

Many times this form of organotherapy is used to mitigate the lowered resistance and general discomfort due to defective ovarian hormone production. For instance how many times have we met the girl or woman who has a period of stress prior to practically every menstrual experience? Whose skin breaks out with acne or eczema? Who may have tonsil or sinus trouble which "lights up" now and then, usually just prior to the menses? Who comes down with grip or something else, usually beginning during the premenstrual week? Who complains of nervousness, asthenia and a sense of impending trouble until the menstrual flow, perhaps long delayed, materializes and is well established? There are thousands of such individuals who in reality are suffering from hypocrinism—involving the ovaries and thyroid, and perhaps others of the endocrine glands—and who will receive lasting benefit from pluriglandular therapy.

A word or two about dosage is in order. This form of treatment is intended to influence the ovarian hormone function. This is a cyclic function, reaching its height just prior to menstruation and dying down to little or nothing thereafter until the monthly period of increased activity is again due. Hence ovarian medication is unnecessary during and for some time after the flow. Here is the routine which I suggest, and emphasis should be laid on the necessity for continuing this measure for several months, for the idea is to affect ovarian endocrine function and this lasts only a short time each month:

Instruct the patient to count 10 days from the onset of the last menses, and during this time to take no capsules. Then one capsule is taken prior to each morning and evening meal during the second 10 days; and a third daily dose is added during the third 10 days, or until the flow starts, when the capsules are stopped.

Following this routine for several months very considerable benefit has accrued in many neuroses of ovarian origin, in amenorrhea, dysmenorrhea and functional pathology due to circulatory imbalance of ovarian origin.

Increasing Fundamental Cell Nutrition

That the greater abdominal glands, the liver and the spleen, exert some subtle endocrine function is accepted by many even though it is still a disputed point. Most

physiologists are agreed that these glands exert a fundamental influence upon nutrition, and the liver by its comprehensive powers of detoxication and bile production is indeed an essential part of the endocrine system. The spleen, too, is claimed to have a part in the regulation of nutrition, especially the assimilation of iron and the maintenance of the intra-cellular digestive processes including those phagocytic digestive powers which make the white blood cells so extremely useful to the organism.

In Europe both hepatic and splenic ootherapy has been in use for 20 or 25 years. A comprehensive study of the literature of these two forms of organotherapy will be found in my book "Practical Hormone Therapy" (Chapters IX and XI). The opinions long held over there are beginning to take hold in this country and the homostimulant action of extracts of these organs is now used by some to enhance those functions which are largely responsible for nutrition. So I offer the following trophogenic combination:

No. 5

Caps. Hepato-Splenic Co.

Desic. Liver Parenchyma
Desic. Spleen Substance aa gr. 2
Powd. Bile Salts gr. $\frac{1}{4}$
Adreno-Spermin Co. (No. 1) gr. 1

The effect of the hepato-splenic combination is reinforced by a small dose of the bile salts and minute doses of the cellulo-tonic combination already referred to on page 36. It has been used with reported good results in conditions of poor nutrition such as tuberculosis, post-febrile malnutrition and cachexia.

I have found considerable encouragement from its use as an adjunct measure in intestinal stasis. Here one expects to find toxemia, anemia and malnutrition accompanied by hepato-biliary stasis and general digestive lassitude. I would not for one minute recommend this formula for the treatment of so broad a disorder as Lane's disease, save only as a means of augmenting other measures. When measures have been taken to support and strengthen the relaxed abdominal walls, when the

accumulations in the dilated bowels are removed and impaction, especially at the hepatic and splenic flexures of the colon, has been disposed of and the patient is put upon a dietetic and hygienic regimen calculated to remove at least some of the causes of the toxemia and asthenia, then, and then only, it is perfectly reasonable and in order to attempt by means of organotherapy to restore the sluggish cellular functions especially of the liver, spleen and adrenals.

It may be hinted by some that the treatment suggested above is likely to be helpful without the organotherapy, and I admit it fully; but I also assert that under such circumstances the removal of anatomical causes has no special beneficial effect upon the long-established results, and we are merely taking away a source of disturbance and letting the body get along as best it can. Undoubtedly the inherent recuperative powers of the organism are better able to respond when the burdens are lightened or removed entirely; but the subtle cellular encouragement to the liver and other abdominal glands certainly favors their more speedy and more thorough restoration. And why should not we give such an individual the benefit of as much physiological assistance as possible? Why merely remove the cause (if possible) and leave Nature to make the best of it? For this reason I urge a consideration of pluriglandular therapy of the kind represented by the formula just mentioned, and know from personal clinical experience that it is by no means an inert remedy.

Sympathetic Sedation in Hyperthyroidism

When the thyroid gland becomes irritable and unruly there immediately results a condition of sympathetic excitability which is largely responsible for the nervous manifestations, the circulatory instability and the heart hurry. Elsewhere I have remarked that with hyperthyroidism we must needs expect hyperadrenia and before long this changes to hypoadrenia when as a result of overstimulation these little glands are worn out.

A hundred and one efforts to cure exophthalmic goiter and hyperthyroidism have left us convinced that it is difficult or impossible to cure the disease itself. We must

find its cause and remove it, then, perhaps, we will get better and more lasting results from our therapy. Incidentally just a word about the surgery of hyperthyroidism. I have seen many cases after operation, in whom the real cause was never found and after surgery the old trouble returned with added dangers and difficulties. Just as this is being written I am telephoned about a case 7 weeks after operation at one of our most important hospitals by a surgeon of repute. The pulse is 140, acetonemia is marked and both patient and physician are at their wits' end.

The successful treatment of thyroidism consists largely in removing the cause rather than its effects! It is quite in order to operate in some cases but even here the surgeon should know as much about etiology as possible. Hyperthyroidism is not solely a thyroid disorder.

A part of the symptomatic treatment of the results of hyperthyroidism properly involves the other endocrine glands and suitable organotherapy certainly helps to control matters. Desiccated pancreas is used by several and it acts thru its antagonistic effect on the adrenals. It is a sympathetic sedative as well as a stimulant to digestion. The pituitary principle also is valuable for its cardio-tonic effect—it slows the pulse and strengthens it (and many times is best used by hypodermic injection daily or as indicated).

Andre Crotti, whose recent book "The Thyroid and the Thymus" (Lea & Febiger, Philadelphia) is indeed a monument to the author's skill and insight into this subject, recommends a pluriglandular formula which includes equal parts of pituitary, adrenal and corpus luteum. I like to add a generous dose of desiccated pancreas and recommend the following combination:

No. 6

Caps. Pancreas Co.

Desic. Adrenal Gld.
Pituitary Gld. (total)aa gr. $\frac{1}{4}$
Ovarian Substance gr. 1
Desic. Pancreas Gld. q. s. ad gr. 5

This formula may be used in the treatment of hyperthyroidism in conjunction with other measures which the exigencies of the case seem to indicate. It has a favorable influence upon the nervousness and the pulse rate

and seems to cause a steadyng effect which is very desirable in these cases. It should always be combined with a thorough-going effort to find and eliminate sources of toxemia (teeth, tonsils, sinuses, alimentary canal and gall bladder, pelvis and elsewhere) and with medication calculated to increase the mineral (alkaline) reserve of the organism. (See Chapter IV.)

The dose of Caps. Pancreas Comp. is from 3 to 6 capsules a day, given preferably an hour or more before meals.

Reinforcing Thyroid Extract

For along time I have given certain mineral salts in conjunction with thyroid extract on what I consider to be very good grounds. Thyroid extract is practically always given in the hope of stimulating metabolism, for hypothyroidism of any degree, from the minor functional insufficiency to the serious conditions of myxedema or cretinism, always means mineral starvation, for the increased systemic wastes rob the body of its alkaline elements and cause acidosis or hypoalkalinity. This is one of the reasons why hypothyroidism is so commonly accompanied by a high urinary acidity and low total solids. It is also why the adipose condition is quite commonly connected with hypothyroidism.

No. 7

Caps. Thyroid Co. Gr. $\frac{3}{4}$
Thyroid Gld. (U. S. P. IX) gr. $\frac{1}{2}$
Calcium Phosphorus q. s. ad gr. 5

I prepare three formulas under the name Caps. Thyroid Comp., each dose containing, respectively, $\frac{1}{2}$, $\frac{1}{4}$ or $\frac{1}{8}$ a grain of standardized U. S. P. IX desiccated thyroid gland with a really useful excipient consisting of a balanced alkaline-saline combination (Calcium Phosphorus Comp.) quite similar to the salts found in the blood. I contend that this "filler" is just as valuable as the thyroid extract in every case where the latter is indicated; and believe that the results from the use of Caps. Thyroid Comp. will be more satisfactory than from thyroid alone, for the obvious reasons just mentioned and more fully considered in the next chapter.

IV

RELATION OF THE MINERAL SALTS TO NUTRITION

AT first thought it may seem strange that this matter is given consideration here; but the reader will shortly see that the subject has much to do with the internal secretions for the very good reason that the internal secretory glands have much to do with metabolism.

Let us recall a few facts. Oxidation, and particularly the gaseous exchanges carried out by the blood, is dependent upon a certain content of alkaline salts in the plasma. In fact it has been aptly remarked that "life is alkalinity, death is acidity." The life-giving processes of the body practically all involve the presence of alkalies; while, on the other hand, the wastes of the organism as well as the toxins produced by disease and abnormal conditions in the alimentary canal, are all acid in reaction or, at least, are alkali robbers. The subject of hypoalkalinity and acidosis is large enough to fill several books of this size; and we can only mention some salient points very briefly.

The acid wastes of metabolism or disease rob the blood and tissues of a part of their alkalies and thus account for the "acidemia" of chronic and infectious diseases. This defensive act on the part of the body—the neutralization of as many acid wastes as possible—brings about an alkali hunger or "demineralization," as the French call it. It is the commonest of conditions in all phases of medical and surgical practice. Yet attention is not given to this subject in the degree that its extreme importance warrants.* Our patients are allowed to con-

*In 1908-9 I did quite a bit of work and wrote a number of articles on the condition known as "acidemia" or systemic hypoalkalinity. I reported a large number of experiments and clinical studies which tended to show that the estimation of the urinary acidity was an easy and satisfactory means of estimating the alkaline balance. I also showed that when indican was present in the urine, more than 70 per cent of the long series studied also showed an abnormally high urinary acidity. A good deal has been written about this since; and I have had many communications from physicians whose eyes had been opened to the importance of routinely considering the urinary acid index.

To facilitate this study in 1908 I devised an acidimeter with which to estimate the acidity of the urine. (Sold by

tinue to follow methods of cooking and eating which deprive them of the very salts that Nature intended should serve to combat the tendency to alkali-depletion common to the "life processes" (in reality properly called "death processes"). Then when conditions reach an extreme we prescribe alkalines, sometimes even by intravenous injection in a belated effort to antagonize this alkali demineralization which accompanies practically every disease process!

Restoring the Mineral Balance

The method of treatment originated years ago and in routine use in France under the name "remineralization" is indeed a rational procedure and while open to criticism as not being so good as accomplishing the same thing by dietetic means (this, of course, is attempted as a part of the associated hygienic treatment of all conditions of this character, but is not sufficiently rapid in its effects to supersede the use of alkaline mixtures), it is a life-saving measure.

The relationship of the ductless glands to mineral metabolism is very important. Several of these organs have been given very essential responsibilities in controlling the "fixation" of the mineral nutriment of the organism. Osteomalacia is said to be of gonad origin. The parathyroids are intimately connected with calcium metabolism and experimental tetany following parathyroidectomy can be controlled by feeding or injecting calcium salts. Rickets is now considered to be just as much an endocrine disease as any metabolic-nutritional dyscrasia. The thymus is considered as exerting some mysterious control over the utilization by the growing organism of both phosphorus and calcium. Undoubtedly a large factor in tuberculosis is connected with ductless

the Taylor Instrument Companies under the "Tycos" mark, the Abbott Laboratories, and other instrument houses both here and abroad). This takes the place of the more cumbersome and expensive burette, though it gives no more accurate service. Its chief advantages being compactness, portability and lower cost. I cordially recommend acidimetry in the study of all chronic disease. When the average normal acidity of 30 to 40 degrees is found to be 80, 100 or even 150 or more degrees, surely this information is of more value than the routine report "Reaction—acid."

glandular function (from both angles, cause and effect) and comparatively recently it has been shown that functional hypoadrenia, commonly present in tuberculosis (asthenia, malnutrition and hypotension are just as pathognomonic of tuberculosis as of hypoadrenia), is in some way responsible for the elimination of calcium in the abnormal quantities noted in tuberculosis, and that the so-called "lime-starved state" is a logical accompaniment of hypocrinism.

So remineralization and organotherapy go hand in hand, the one supplementing the advantages of the other in a very tangible manner.

Supplementing Endocrine Function

Again it so happens that an important part of the chemical service rendered to the organism by the endocrine glands is the maintenance of the metabolic processes and the destruction of toxins by oxidation. We all know how badly disorganized is the cell chemistry in thyroid insufficiency. Hence it should be correct to deduce from this that every case of hypothyroidism is likely to be suffering from mineral starvation; and clinically this is absolutely a fact. It is just as true in the minor thyroid insufficiencies that are overlooked every day, as in myxedema or cretinism, and the only difference is one of degree.

Let me repeat this for emphasis: Subthyroidism means retarded cell metabolism. This, in turn, means a concentration of an abnormal amount of wastes which, because of their affinity for alkalies, deplete the body's reserve of these minerals. Or as I have remarked elsewhere: "Hypothyroidism means suboxidation; suboxidation means toxemia; toxemia means hypoalkalinity and hypoalkalinity means mineral starvation or demineralization."

Surely the correction of this ultimate condition is just as rational as the augmentation of the endocrine deficiency which caused it. In other words, we can advantageously supplement thyroid therapy (and other organotherapeutic measures) with an attempt to replace the mobile mineral reserve of the organism—remineralization. This should be the rule in all chronic disease,

especially those which involve metabolism and nutrition—not merely such notable types of systemic hypoalkalinity as diabetes mellitus, "rheumatism," etc. Incidentally it is surprising how often a very small dose of thyroid supplements this mineral therapy.

Several methods are available. It is very easy to recommend a package of the "Arm & Hammer" brand and to suggest 60 to 100 grains a day in plenty of water remote from meals; and this helps, sometimes amazingly. In France they use bone-dust, oyster-shell powder and other "organotherapytic" mineral preparations. I do not believe that these salts are any the more easily assimilated than the ordinary chemicals of commerce. For instance, calcium phosphate is actually made commercially from bone ash and, therefore, according to some, should be called an "organic" mineral salt.

Several formulas have been recommended in the remineralization procedure. For a long time I used a proprietary called "Metabolets" made in New York. I have used Trunecek's so-called "artificial serum," with slight modification. This is said to be "the normal blood salts in proper proportion"; and the formula is: Sod. Chlor. 0.8 gm., Sod. Sulphate 0.08, Magnes. Phos. 0.3, Sod. Carb. 0.3, Sod. Phos. 0.25 and Calc. Phos. 0.25. This is an average dose and is given three times a day especially in arterial degenerations.

Calcium Phosphorus Compound

I personally use and recommend a combination which I have called "Calcium Phosphorus Comp." I believe that its addition to thyroid extract is particularly rational and my "Caps. Thyroid Comp." is a carefully standardized (U. S. P. IX) preparation diluted with this remineralizing combination of salts. The formula is as follows: Magnes. Phos. 1, Calc. Phos. 4, Calc. Glycero-phos. 4, Potas. Bicarb. 16, Soda Bicarb. 25 and Sod. Chlor. to make 100 parts. The potash salt is indeed an advantageous addition despite its present abnormal expense; and I prefer to replace the more strenuous sodium carbonate with the bicarbonate which is not so irritating to the stomach, and, too, it is not deliquescent like the carbonate and is easier handled in a dry form.

Calc. Phosphorus Co. is the standard diluent in my laboratory, taking the place of the usual milk sugar because it has a distinct therapeutic value, especially in conditions in which it is advisable to prescribe organotherapy. Indeed, many of my friends are now demanding it alone to supplement their treatment of numerous disorders and before long I may be offering a tablet as an adjuvant to other preparations from this laboratory.

Since writing the above, the requests for a product like the remineralizing combination just referred to have made it seem advisable to put out a tablet of this useful alkaline-saline formula. While the sole function of my laboratory is to develop organotherapy, it is not out of place to co-operate with those who are interested in my work and preparations; and despite the fact that Calcium Phosphorus Comp. is by no means a glandular product it is indeed useful when given in conjunction with pluriglandular medication. It is not easily obtainable on the market and I have many times put up 9-grain capsules of my excipient as a favor to those who wanted to increase the dose over the amount which may be in the organotherapeutic capsules.

So I have had prepared some friable tablets of one gram (15 grains) and call them "Tabs. Calc. Phosphorus Comp." (Harrower)—when prescribing write the words as above to avoid conflict with "calcium phosphate"—and recommend two to six of these tablets as a suitable daily dose, one to three of them being crushed and taken with a full glass, or more, of water, at least three hours after or one hour before meals.

A TEST FOR THYROID SECRETORY FUNCTION

A KNOWLEDGE of the endocrine activity of the various glands would be a very convenient addition to our diagnostic information if there only were some way of measuring it. We know well enough, or should know, when an individual has a prominent increase or decrease in the functional activity of some of the endocrine glands, but the less prominent forms are not so easily estimated. Too often they are altogether overlooked.

During the several years that I have devoted myself largely to the study and diagnosis of disorders of the ductless glands and conditions in which the endocrine side is presumed to be prominent, I have many times wished that I could have a chart of the various endocrine capacities just as we can get a report on the elimination of the different urinary solids or a record of the several facts about the circulation—the pulse, systolic and diastolic pressures, pulse pressure, etc. Like all others I have found those whose response to thyroid therapy was both unexpected and undesirable, and out of these failures I have devised a method of testing or measuring comparatively the thyroid secretory capacity.

The Differentiation of Goiter

This information is of much service, especially as we recall that there are two distinct varieties (variously subclassified) of goiter—(1) the simple enlargement of the gland which is an effort on the part of the body to supply an increased demand for the particular product which may be deficient or used to excess, and (2) the pathological hypertrophy due to some extra-glandular cause which brings with it varied symptoms of hypercrinism. The former, or simple, goiters represent an attempt on the part of the organism to render it the best service possible and usually are benefited by a course of treatment which includes the administration of thyroid stuff thus supplying the need, in part at least, and rendering the friendly glandular enlargement unnecessary. In such cases thyroid extract, iodine and other similar remedies speedily reduce the goiter. (See page 35.)

In the other class of cases, however, conditions are vastly different. Some stimulus, usually toxemia from a focal infection and occasionally deranged function on the part of some other of the allied endocrine glands particularly the adrenals, is driving the thyroid faster than usual. It is more sensitive and hence more unruly. The hypertrophy differs materially in origin and, naturally, in its treatment. What would be beneficial in simple goiter, would be detrimental in hyperthyroidism.

The differentiation of the advanced stages of these conditions is not difficult but, alas, it is of less value, for then conditions have gone well past the early, functional stages. If we can find a way of discovering the thyroid sensitiveness or susceptibility to hormone and other influences, we have differentiated between latent hypo- and hyper-thyroidism, and accomplished something of real value.

This did not appear to be a difficult task in view of the occasional reactions we have noticed in connection with thyroid therapy; so I have devised a method whereby definite, step-ladder doses of thyroid gland with a suitable excipient, are given in a uniform and routine manner, while a careful and regular study is made of the pulse and other reactive symptoms. At first I was quite surprised at the information thus obtained. The charts were most interesting and many times I found out that in a given case conditions were quite considerably different from what I had supposed.

The following statement is printed on a convenient slip together with a chart upon which the patients record the findings, and is handed to them with a small box containing the materials for the test:

A Method of Thyroid Function Testing

Instructions

Each package of "Thyroid Testing Capsules" contains 12 capsules of three graduated strengths and sizes. A pulse chart accompanies each, with explicit instructions as to how to fill out the record.

After the consultation, at which the first pulse-counting is done and recorded, the patient counts the pulse

again at 6 and 9 o'clock; and the following morning commences to take the four small capsules at 8, 10, 12 and 2 o'clock with a swallow of water, recording the pulse five times a day—at 9, 12, 3, 6 and 9 o'clock. On the second day the four medium-sized capsules are taken at similar hours and the pulse is again recorded under as nearly identical conditions as possible, and at the same hours.

During the third day the four large capsules are taken at the same hours as previously and the pulse is again recorded as before. The fourth day, or the "first day after" finishing the ingestion of the capsules the pulse is recorded as before and again during the forenoon of the fifth day when the chart is completed (and plotted, if convenient), the physician is consulted and the data thus secured carefully studied.

It is important to watch for symptoms such as irritability (temperamental or nervous), twitchings (of the eyelids, lips, fingers, etc.), breathlessness and other nervous manifestations. If it should happen that on the second or third days these symptoms are present and prominent, the remaining capsules should not be taken; but the chart is completed, while on its reverse side a brief statement is made of the symptoms, giving the time of onset and other related facts.

Reading the Pulse Charts

Some day I am going to publish a number of these plotted pulse curves with the other accompanying clinical and later therapeutic findings. It is most interesting. In the meantime to facilitate the use of this thyroid function test by my colleagues I will give the gist of my conclusions.

Ordinarily the experimental thyroid medication makes a slight difference to the pulse rate in the normal individual, rarely, however, does it reach above 90 and then only under the immediate influence of the ingested thyroid, i. e., it falls back again the day after. In hypothyroidism the pulse is usually lower than usual and the reaction following the thyroid medication is little or nothing, in other words the apathy is visible on the chart. In the various stages of thyroidism, the pulse

findings are characteristic, the greater the susceptibility the wider the range. The evidence of an irregularly appearing chart with the pulse 100, 110 or more is very definite, and as previously noted when the patient sees this early in the test, the balance of the capsules is omitted. Again in thyroidism the pulse does not immediately return to its norm, and in fact it may be accelerated during several days after, in which case it is well when it seems advisable to omit a part of the capsules to extend the record of the pulse figures over the sixth and seventh days.

No.	PULSE CHART												Date					
	Name			Address														
	DAY BEFORE			FIRST DAY			SECOND DAY			THIRD DAY			DAY AFTER TEST			2D DAY AFTER		
	3	6	9	9	12	3	6	9	9	12	3	6	9	9	12	3	6	9
160																		
150																		
140																		
130																		
120																		
110																		
100																		
90																		
80																		
70																		
60																		
50																		

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The test is greatly facilitated by the printed instructions and chart as well as the use of a uniform and standard dosage of thyroid. In other words, it is an advantage to pay a few cents—thirty-three in fact—for a ready-to-use test, than to make it up or prescribe it as needed. I find a marked advantage in the finished marketable test over that prepared extemporaneously in the same laboratory and used before the charts were printed or the accurately standardized series of capsules was made.

With the information thus secured it is possible to render a much more satisfactory service to the patient, and, too, it gives one a feeling of comfort in the treatment of goiter which is well worth while.

VI

SPECIAL PLURIGLANDULAR COMBINATIONS

AS explained in the introductory remarks, the object of this laboratory of applied endocrinology is to broaden organotherapy; and it is my opinion that this will be done more by discovering the mysteries of the relations of the endocrine glands and the advantages of combining their extracts, than in any other way.

The facilities of this laboratory have been placed at the disposition of the profession and a surprisingly large number have availed themselves of this opportunity. Scores of various combinations of gland products have been made, and modified, and made again. A number of the most interesting of these special formulas are given here. I am taking the liberty of drawing attention to their therapeutic possibilities and believe that the good results attained by a few will be repeated by many who heretofore were not aware that we produced anything save the stock pluriglandular formulas discussed previously (Chapter III).

Let it be understood that any combination will be made on request. These special formulas can be changed to suit your own ideas. Those enumerated in the following pages appear to have a reasonable basis of usefulness and are known to be serviceable.

Simple Goiter

In the previous chapter I have called attention to a test for the differentiation of simple hypertrophic goiter and thyroidism with or without marked glandular enlargement, and emphasis was laid upon the diversity of the treatment. Where thyroid enlargement is the result of an attempt of the system to meet certain unusual demands for the thyroid stimuli, the gland becomes enlarged in order to render the larger service required of it. There are, of course, many other conditions to be considered in the study of goiter; but we may safely say that many a simple goiter will respond favorably to thyroid feeding and to the administration of iodine. I think I have an excellent combination which serves the double purpose of offering the organism a suitable

amount of thyroid and a convenient form of iodine, and believe that the added hematinic virtues of the iodide of iron as well as the leucocyte- and resistance-stimulating effect of nuclein make a far better preparation than plain thyroid alone.

Special No. 18

Caps. Iodized Thyroid Co.

Thyroid Gld. (U. S. P. IX) gr. $\frac{1}{4}$

Ferrous Iodide gr. $\frac{1}{4}$

Ac. Nucleinic (nuclein) gr. $\frac{1}{4}$

Calcium Phosphorus Co. q. s. ad gr. 6

Some may care to have still less thyroid and no nucleic acid, in which case another similar formula may be prescribed:

Special No. 19

Caps. Iodized Thyroid Co. without Nuclein

Thyroid Gld. (U. S. P. IX)

Ferrous Iodide aa gr. $\frac{1}{4}$

Calcium Phosphorus Co. q. s. ad gr. 6

One or the other of these combinations is recommended as a very useful part of the treatment of simple goiter, and from 2 to 5 doses may be given daily, depending upon circumstances. In anemic girls with obvious thyroid enlargement and no evidence of thyroidism (after the Thyroid Function Test has been made) the enlargement sometimes "melts away" in a few weeks. However, always in such a case a careful search should be made for hidden causes of the thyroid hypertrophy and quite often it may be that dysovovarism is an underlying cause which, of course, may be better treated with another similar remedy, my Caps. Thyro-Ovarian Comp., for instance. (See page 18.)

Quite often I have recommended inunction of the thyroid area with Iodex ointment every evening with benefit. I have also used an ointment of the yellow iodide of mercury. Elimination, remineralization and good hygiene are also a part of the treatment of all cases of goiter.

Hepato-Biliary Insufficiency

A very simple but distinctly useful combination is that of desiccated hepatic substance with the active principles of the bile salts, thus:

Special No. 22

Caps. Bile Salts Co.

Powd. Bile Salts

Desic. Hepatic Substance aa gr. 3

The clinical indications for the administration of either of these organotherapy remedies are well known. The combination is superior to the single ingredients. In functional liver troubles, intestinal stasis, biliary insufficiency, gall stones and sluggish bile flow, as well as in more serious disorders of nutrition and particularly tuberculosis, a formula of this character can be recommended with benefit. As a means of reinforcing the cellulo-tonic effect of Caps. Adreno-Spermin Comp., referred to in Chapter III (p. 11), two or three daily doses of Caps. Bile Salts Comp. help to clear up the sallow skin and loosen up the liver secretions in a very nice way.

The proper dose of Caps. Bile Salts Comp. is "enough"! Usually three capsules a day suffice, taken preferably remote from meals with a little water. Again two capsules at night may be quite sufficient, while early in the treatment of some old chronic cases where real "dynamite" is needed to awaken the liver and the patient has been accustomed to cathartics of all kinds for years, five or even six doses a day for a while may be advisable. Give enough to cause two or three stools a day, and after a week have the patient gradually reduce the dosage until only two capsules are being taken at night. I recommend that this small dose be continued for several months.

Intestinal Indigestion

Another very similar formula is:

Special No. 23

Caps. Pancreatin-Bile Co.

Pancreatin (U. S. P. IX)

Powd. Bile Salts

Desic. Hepatic Substance aa gr. 3

a part of the hepato-biliary extracts being replaced with an active pancreas preparation. The indications are virtually the same as for the previous formula, though perhaps this addition of pancreatin makes this combination more suited for the control of conditions in which intestinal indigestion, alimentary putrefaction, fetid stools (often light-colored and sticky) and mucous colitis are

prominent symptoms. The dosage of *Caps. Pancreatin-Bile Comp.* is one or two capsules two or three hours after food; and of course the treatment which favors a clean bowel should be prescribed simultaneously.

A Remedy in Paralysis Agitans

The parathyroid glands have been shown to serve the body by their faculty of destroying toxins which have a predilection for the nervous system. There has been a good deal of controversy about the pathology of the parathyroids in paralysis agitans, tetany, and other conditions of similar character. Good results have been secured by parathyroid therapy in these disorders and while the prognosis in advanced cases is not especially good, there have been occasional results that would not be believed when they were reported; and some writers have come in for quite a little criticism because they reported splendid control of all the symptoms which characterize Parkinson's disease.

Here is a formula which you may care to use:

Special No. 24
Capa. Parathyroid Co.
 Desic. Parathyroid Gld. gr. 1-20
 Spermin Extr. (from Gonads) gr. 1
 Powd. Bile Salts gr. 1½
 Calcium Phosphorus q. s. ad gr. 5

This is superior to parathyroid substance alone for three reasons: (1) there is a well-established functional relationship between the parathyroids and the liver, (2) practically every case of paralysis agitans would be the better of the functional liver stimulation which the supplementary bile salts favor, and (3) the cellulo-tonic effect of spermin is always useful in senility and this disease is essentially of waning cellular activity.

I have had occasion to put up this formula with 1-200 grain of atropine sulphate to each capsule, and this has made it of considerably greater value. The amount of the alkaline-saline combination used in this formula may be augmented by giving increased amounts.*

The Control of Functional Hypertension

The conception that certain forms of functional hypertension are either of endocrine origin or amenable to

*See note at end of Chapter IV.

measures calculated to modify endocrine activity, has been given study by a number of individuals and an opinion is gaining ground that when such organic disorders as renal disease, cardiac hypertrophy or arteriosclerosis can be ruled out, the hypertension may be due to irritation of those organs responsible for the maintenance of the sympathetic manifestations, including the blood pressure. The French admit an adrenal form of hypertension; and I am personally convinced that toxemia, bacterial, intestinal or drug (caffeine, morphine or alcohol, for instance), is capable of stimulating the adrenal system and thus producing the high pressure. This may be merely a suspicion; but it is seemingly confirmed by the sometimes remarkable depressor effects of desiccated pancreas given internally. This exerts an anti-adrenal effect and it is conceivable that in the cases in which this remedy is so strikingly useful, the adrenals have been overworking and the sedative influence of the pancreas suffices to reduce this.

Some time ago I initiated a series of clinical experiments with several organo-therapeutic formulas for the control of functional hypertension, and submit here four formulas, somewhat similar to one another, which have been developed as a result of these experiments.

Special No. 27

Caps. Thyro-Pancreas Gld. Co.

Desic. Pancreas Gld. (total) gr. 3
Thyroid Gld. (U. S. P. IX) gr. 1-12
Calcium Phosphorus Co. q. s. ad gr. 5

Special No. 28

Caps. Thyro-Pancreatin Co.

Pancreatin (U. S. P. IX) gr. 4
Thyroid Gld. (U. S. P. IX) gr. 1-12
Calcium Phosphorus Co. q. s. ad gr. 5

Special No. 29

Caps. Thyro-Pancreas Co. with Spermin

Desic. Pancreas Gld. (total) gr. 2
Thyroid Gld. (U. S. P. IX) gr. 1-12
Spermin Extr. (from Gonads) gr. 2
Calcium Phosphorus Co. q. s. ad gr. 5

Special No. 30

Caps. Thyro-Pancreas Co. with Ovary

Desic. Pancreas Gld. (total) gr. 2
Thyroid Gld. (U. S. P. IX) gr. 1-12
Ovarian Substance gr. 2
Calcium Phosphorus Co. q. s. ad gr. 5

All of these formulas have given fairly good results; the last has proved particularly useful in the functional hypertension, sometimes accompanied by adiposity, in adiposity, in women at or just beyond the menopause.

While the principal objective in the use of any of these formulas has been the control of the high blood pressure, it must not be forgotten that this is usually an incidental result. Caps. Thryo-Pancreas Gland Comp. and the similar but different Caps. Thryo-Pancreatin Comp. are both useful in hypothyroidism in elderly persons especially where digestion in the intestine is not good.

The by-effects of the addition of the spermin-bearing extract and total ovary in Nos. 29 and 30, respectively, are well worth while, and as a gonad stimulant they both have their place. In fact many good reports of the benefit from these two formulas lead me to hope that we are "on to" a really useful measure in the adjunct control of disordered chemistry with high blood pressure.

A Post-febrile Reconstructant

Following acute infectious diseases, especially in children and young people whose powers of resistance are none too good, certain forms of "nutritive organotherapy," if we can coin this term, are particularly advantageous. Lecithin, "the most easily assimilated form of phosphorus," is indicated in such cases and the definitely established effect of nuclein (nucleinic acid) in increasing leucocytosis and the powers of resistance adds to its value. Hemoglobin is also especially valuable for its hematopoietic and reconstructive capacity far exceeds that of many of the other less easily assimilated and more commonly used forms of iron. To such a splendid combination we can add a small dose of spermin (from the interstitial cells of Leydig) for its dynamic or musculo tonic effect and we have an organotherapeutic reconstructant that "delivers the goods"!

Special No. 35

Caps. Nuclein-Hemoglobin Comp.
Ac. Nucleinic gr. $\frac{1}{4}$
Lecithin gr. 1
Spermin (Leydig cells) gr. 1
Hemoglobin q. s. ad gr. 5

A preparation like this combines several purely physiological stimulative effects all of which are especially needed following any severe illness whether acute or chronic, in young or old. This will be found far superior, because more rational, than the old-fashioned tonics like I. Q. and S. A hundred capsules, given in doses of three or four capsules per day, will augment the re-establishment of those essential functions which have suffered from the fever and toxemia from which the patient is convalescing.

Hemoglobin in Anemia

The market is filled with many forms of iron, from the old-fashioned Blaud's mixture to various "organic" irons which are recommended in the treatment of anemia. Certainly iron is a valuable remedy for anemia, provided that the iron is both absorbable and assimilable, features which are not at all true in connection with many of the customary iron salts in current use. Personally I prefer the intramuscular injection of iron cacodylate as a first-class remedy for anemia and malnutrition, for the combination with arsenic is a splendid one. The next best form of iron, and the very best form for internal use is the so-called "ferrum sanguinis" or hemoglobin. This is indeed organic iron and it is rapidly and constantly absorbed without constipation or indigestion. It has all the advantages of other salts of iron—ferric and ferrous—and there must be some other effect than merely that of the iron molecule, for hemoglobin is considerably better than most other hematinic tonics. Yet is not so very much used in this country.

At the request of a prominent internist up-state I prepared for him the following formula:

Special No. 37
Caps. Hemoglobin Co.
Repurified Hemoglobin gr. 3
Medullary Substance gr. 1
Thyroid Gld. (U. S. P. IX) gr. 1-16
Calcium Phosphorus Co. q. s. ad gr. 6

This was used with considerable success, especially in young persons where there seemed to be evidence of a minor form of hypothyroidism complicating the anemia and malnutrition. In the anemic, pasty youngster whose resistance is low, such a remedy is excellent.

Later some physicians asked to have a similar preparation without any thyroid extract, and it was suggested that the addition of a medium dose of spleen extract ought to be good, for there is quite a little in the literature on the hematinic and reconstructive value of this substance. So another hemoglobin combination was made which is called **Caps. Spleno-Hemoglobin Comp.:**

Special No. 36
Caps. Spleno-Hemoglobin Co.
Repurified Hemoglobin gr. 3
Desic. Spleen Substance gr. 2
Calcium Phosphorus Co. q. s. ad gr. 6

I have had some fine reports from those who have used these formulas, and I am not surprised for theoretically they should be "winners."

The dose is 3 or 4 capsules a day, preferably taken just before meals. In severe anemia a larger quantity of **Caps. Spleno-Hemoglobin Comp.** may be given for some weeks; and, on the other hand, in the hypothyroid anemia or where **Caps. Hemoglobin Comp.** is advised in children or adults with an obvious thyroid insufficiency, the amount of thyroid may be increased by administering **Caps. Thyroid Comp.** ($\frac{1}{8}$, $\frac{1}{4}$ or $\frac{1}{2}$ gr. of thyroid) simultaneously, and the accompanying alkaline mineral salts are by no means a disadvantage in this particular class of cases.

Mammary Extract in Menorrhagia

One of the most peculiar features of organotherapy is the antagonism of the internal secretions of the mammae and ovaries. It is well established that the administration of mammary substance antagonizes ovarian function and thereby reduces pelvic congestion, uterine enlargement and abnormal menstrual bleeding. Some writers, especially of the Petrograd school, believe that mammary therapy reduces uterine fibroids and even cures them; but while I have seen many good results in the control of menorrhagia I have not seen any remarkable effects upon new growths of the uterus.

Several formulas with mammary substance as their basis have been prepared in this laboratory, three of which are mentioned here. The first contains these ingredients:

Special No. 38

Caps. Mamma-Ovary Co.

Mammary Substance gr. 2 $\frac{1}{2}$
Ovarian Substance gr. 1
Thyroid Gld. (U. S. P. IX) gr. $\frac{1}{8}$
Calcium Phosphorus q. s. ad gr. 5

Despite the fact that these first ingredients are theoretical antagonists, the combination is useful in moderate menorrhagia with dysmenorrhea and simultaneous evidence of dysovarism, such as a difficult menstrual onset, or an abnormally short interval between the menses. Sometimes this formula may be alternated with Caps. Thyro-Ovarian Comp. in ovaro-uterine disorders which lean to menorrhagia or where the clinical results from this latter stock formula leave something to be desired.

Caps. Mamma-Ergotin Comp., prepared for a prominent Oakland gynecologist, contains a medium dose of Bonjean's ergotin, thus:

Special No. 39

Caps. Mamma-Ergotin Comp.

Mammary Substance gr. 3
Ergotin (Bonjean) gr. $\frac{1}{8}$
Calcium Phosphorus q. s. ad gr. 5

This is not merely a symptomatic regulator of menorrhagia, but it is simultaneously modifying the underlying conditions which are responsible for the excessive hemorrhage.

Still another formula of this type, in which the uterotonic effect of the above combination is reinforced by the addition of total pituitary gland:

Special No. 40

Caps. Mamma-Pituitary Co.

Mammary Substance gr. 2 $\frac{1}{2}$
Ergotin (Bonjean) gr. $\frac{1}{8}$
Pituitary Gld. (total) gr. $\frac{1}{8}$
Calcium Phosphorus q. s. ad gr. 5

There is an optimum manner in which to administer preparations of mammary substance. I usually recommend a similar procedure to that outlined for the dosage of Thyro-Ovarian Comp. (see page 19), but instead of omitting during the menses I push the dosage then. For ten days after all flow has ceased the capsules are not taken, then doses of 2 or 3 capsules a day are taken for 10 days, more or less depending upon the length of the intermenstrual period. Three or four days before the flow is expected and during the flow, the dosage is

increased as may seem advisable, 6 or more capsules being quite in order.

Extreme menorrhagia is best treated with the Caps. Mamma-Pituitary Comp., and even a hypodermic of pituitary solution or cotarnine hydrochloride may be needed before the excessive flow is under control.

Senility, Asthenia and Prostatic Disease

The homostimulant effect of extracts of the gonads has been proved time and again since Brown-Sequard's original experiments. It is possible to increase waning gonad function just as we can augment the endocrine function of other glands. A distinction must be made between the internal and external secretory function of these glands. Organotherapy may increase the production of the seminal fluid, or it may not; it certainly exerts a very distinct effect upon those general cellular functions which are the result of the internal secretion of the testes. This means that while impotence may not always be so remarkably benefited as the charlatans insisted so vociferously when they "caught on" to what Brown-Sequard was doing (and thereby gave scientific organotherapy a bad name for thirty years or more), the dynamogenic effect or the influence on general cell-tone is undoubtedly.

The essential endocrine part of the testes, the interstitial cells of Leydig, which correspond in a sense to the corpora lutea of the ovaries, contain the active principle called "spermin," discovered and exploited by Prof. von Poehl of Petrograd. This stimulates oxidation and muscular power, and is the essential therapeutic element in orchic substance, didymin and desiccated testicular substance.

An active product of these cells is prepared under the name Caps. Leydig Cell Comp., and a proportion of this substance representing over 20 grains of the fresh glandular tissue is found in each dose or the equivalent of four tablets of the testicular product quite generally known to the profession. The small dose of thyroid is added on the principle that in asthenic individuals as well as in elderly men there is a general hypocrinism present and, besides, a prominent New York physician

suggests that a small daily dose of thyroid in elderly persons "helps to keep the arteries soft"! Finally calcium glycerophosphate is superior to milk sugar as an excipient (even though it costs several times as much) for it is a constructive mineral which is easily absorbed and which it is claimed supplies much needed and thoroughly assimilable phosphorus to the nervous tissues.

I have been much pleased with the reports on Caps. Leydig Cell Comp.:

Special No. 41

Caps. Leydig Cell Co.

Spermin Extr. (Leydig cells) gr. 2*

Thyroid Gld. (U. S. P. IX) gr. 1-16

Calcium Phosphorus q. s. ad gr. 5

Peculiarly enough this formula was originally prepared for a prominent urologist for the treatment of certain forms of prostatic hypertrophy, especially that type of enlargement not accompanied by an infection, that is not infrequently found in men whose gonad activity is on the wane, and which is not the result of a new growth. It is conceived that this prostatic enlargement might be of a compensatory nature, the prostate attempting to supplement the lessened service rendered by the testes. Suffice it to say that in addition to general cellular stimulation such as one might expect from the homostimulant action of such a formula, I have definite information that it has also caused decided benefit to the most common symptom of prostatic enlargement—difficult and frequent micturition.

Another similar formula contains an extract of lymphatic glands for reasons which I am not quite sure of. It is said, but not proved, that lymphatic substance is of benefit in conditions of gonad insufficiency such as we have just been considering.

Special No. 42

Caps. Leydig Cell Lymph Co.

Spermin Extr. (Leydig cells)*

Desic. Lymphatic Gld. aa gr. 2

Thyroid Gld. (U. S. P. IX) gr. 1-12

Calcium Phosphorus Co. q. s. ad gr. 6

Another remedy for the difficulties accompanied by prostatic disease and the cellular insufficiencies of sexual

**This is the equivalent of nearly 20 grains of the Leydig elements of fresh sheep's testes.

neurasthenia contains the tonic principles just referred to together with desiccated prostate gland substance.

There has been some controversy over the merits of prostatic organotherapy, but this is not unusual. Clinically it has helped, it may again!

The addition of nuclein is certainly of value in conditions of lowered resistance.

Special No. 48
Caps. Prostate Gland Co.
 Desic. Prostate Gld.
 Spermin Extr. (from Gonads)
 Desic. Lymphatic Glds. aa gr. 1½
 Acid Nucleinic gr. ½
 Calcium Phosphorus Co. q. s. ad gr. 6

The dosage of these three remedies is usually one or two capsules three times a day just before meals. Since the effects are expected to be of an endocrine nature, and unlike the rapid and fleeting stimulation of strychnia and other similar drugs, the extracts must be taken for some weeks or months in order to educate or re-establish lost or deficient hormone-producing functions. Where organotherapy is advisable for moderately long periods, I usually advise the omission of the remedy entirely during every third or fourth week.

Hemophilia and Lymphatic Children

In the occasional child or, for that matter, the adult who exhibits a lymphatic tendency, bleeds easily and is also poorly nourished and anemic, the following hemostatic and reconstructive combination has been recommended:

Special No. 43
Caps. Lymphatic Gland Co.
 Desic. Lymphatic Glds. gr. 2
 Spleen Substance gr. 1½
 Thyroid Gld. (U. S. P. IX) gr. 1-16
 Calcium Lactate q. s. ad gr. 6

It will be seen that this formula "sounds well" theoretically, and while in difficult cases of this type it is neither easy nor right to promise results, for practically never can we be assured of all that is wrong with the patient, at least we can administer a preparation of this character with reasonable prospects of favorable results.

The suggested dose is three or more capsules per day, just before meals; and where the anemia is marked it

may be well to add a similar dose of **Caps. Hemoglobin Comp.**, mentioned previously.

Definite Pituitary Disease

Fortunately well-defined disease of the pituitary gland is not common. Hypopituitarism or Froehlich's syndrome is a disease with a discouraging outlook. The only hopeful treatment at present recommended (by Cushing, Bartels and other authorities) is gland feeding. There are several possible pituitary preparations, for the gland has at least three distinct histological portions. The total gland is often used; so is the anterior lobe or the essential glandular portion of the hypophysis. The former contains a principle which influences carbohydrate metabolism, while the latter contains a quite different substance which stimulates growth and the development of gonad function. For several reasons which I need not enumerate I suggest the following **Caps. Pituitary Comp.** which is a balanced combination of an extract of the total gland and also of the anterior lobe with **Calcium Phosphorus Comp.**:

Special No. 47

Caps. Pituitary Co.

Pituitary Gld. (total)

Pituitary Gld. (anterior lobe) aa gr. 1 $\frac{1}{4}$

Calcium Phosphorus q. s. ad gr. 5

Please note that the above figures, and for that matter all the preceding figures in this book, refer to grains of finished desiccated gland substance and not to fresh substance. This distinction is very necessary in figuring both dosage and costs. Usually the formulas as outlined represent one average dose, to be repeated two or more times a day. In the case of pituitary feeding it must be continued for long periods, the above formula or **Caps. Antero-Pituitary Comp.** containing also thyroid and thymus extracts (see page 14) being given two or three times a day before meals.

VII PRICES

THE stock formulas from this laboratory are distributed thru the regular trade channels, and physicians may prescribe them thru their usual pharmacists who, in turn, obtain them either direct or from their jobber. The following prices are for retail and the patient should not pay more. A discount of 20% is given to physicians by this laboratory or the druggist who may supply him.

Different arrangements are necessary with experimental or special formulas. Ofttimes these are not even in stock at the laboratory and have to be made to desired to prescribe any of these it will be necessary to so inform your pharmacist and have him order direct. These formulas are never sold thru the wholesale trade, and are only stocked by certain druggists who do so by arrangement with, and for the convenience of, certain interested prescribers.

Special formulas other than those listed here will be made with pleasure. Any quantity may be ordered, though it is preferred to make a minimum of 300 capsules of a given formula. Any formula will be changed on a similar basis, and the charges will be in harmony with those mentioned below and with the costs of the desired ingredients. Modified stock formulas are, of course, special formulas.

Your patronage, and thus your co-operation in maintaining and developing this laboratory of applied endocrinology, will be much appreciated; and suggestions or criticisms will be gladly welcomed.

STOCK FORMULAS

No	Name.	Indication	gr	50	100
1	Caps. Adreno-Spermin Co.	Dynamogenic	v	\$1.50	\$2.50
2	Caps. Antero-Pituitary Co.	Development	v		3.75
3	Caps. Placento-Mammary Co.	Galactogenic	v	2.00	3.50
4	Caps. Thryo-Ovarian Co.	Ovaro-Uterine	v	2.00	3.50
5	Caps. Hepato-Splenic Co.	Trophogenic	v		3.00
6	Caps. Pancreas Co.	Hyperthyroidism	x	1.50	2.50
7	Caps. Thyroid Co. (gr. $\frac{1}{2}$)	Hypothyroidism	x	1.00	1.75
8	Caps. Thyroid Co. (gr. $\frac{1}{4}$)	Hypothyroidism	x	1.00	1.75
9	Caps. Thyroid Co. (gr. $\frac{1}{2}$)	Hypothyroidism	x	1.00	1.75
10	Thyroid Testing Capsules	Function Test	3 t.		1.25
11	Tabs. Calc. Phosphorus Co.	Hypoalkalinity	xv	1.00	1.50

Too much emphasis can not be laid on the statement made previously to the effect that Special Formulas, including those listed below, are not on regular sale thru the trade. Do not expect your druggist to have them or to know of them. You can order them direct at the net prices below or you can have them sent to a designated pharmacy for convenience in prescribing, but the druggist can not get them from his wholesaler.

SPECIAL FORMULAS

No	Name	Indication	gr	100
18	Caps. Iodized Thyroid Co.	Simple Goiter	vi	\$2.75
19	ditto without Nuclein	Simple Goiter	vi	2.25
22	Caps. Bile Salts Co.	Biliary Insufficiency	vi	2.00
23	Caps. Pancreatin-Bile Co.	Intestinal Indigestion	vi	2.50
24	Caps. Parathyroid Co.	Paralysis Agitans	v	3.00
27	Caps. Thryo-Pancreas Gld. Co.	Hypertension	v	2.25
28	Caps. Thryo-Pancreatin Co.	Hypertension	v	2.50
29	Caps. Thryo-Pancreas Co. with Spermin	Hypertension (men)	v	3.00
30	Caps. Thryo-Pancreas Co. with Ovary	Hypertension (wom)	v	3.00
35	Caps. Nuclein-Hemoglobin Co.	Postfebrile Convalesc.	v	3.50
36	Caps. Spleno-Hemoglobin Co.	Anemia	vi	3.00
37	Caps. Hemoglobin Co.	Hypothyroid Anemia	vi	3.00
38	Caps. Mamma-Ovary Co.	Dysovarism	v	3.00
39	Caps. Mamma-Ergotin Co.	Menorrhagia	vi	3.00
40	Caps. Mamma-Pituitary Co.	Menorrhagia	vi	3.50
41	Caps. Leydig-cell Co.	Senility, etc.	v	3.00
42	Caps. Leydig-cell Lymph Co.	Senility, etc.	vi	3.50
43	Caps. Lymphatic Gld. Co.	Hemophilia	vi	3.00
47	Caps. Pituitary Co.	Hypopituitarism	v	3.00
48	Caps. Prostate Gld. Co.	Prostatic Disease, etc.	vi	3.50

Prescribe these products by their full name—kindly specify "Harrower." Order by name or number (special formulas by both name and number) direct or through your local druggist. Write for specific information when you wish.

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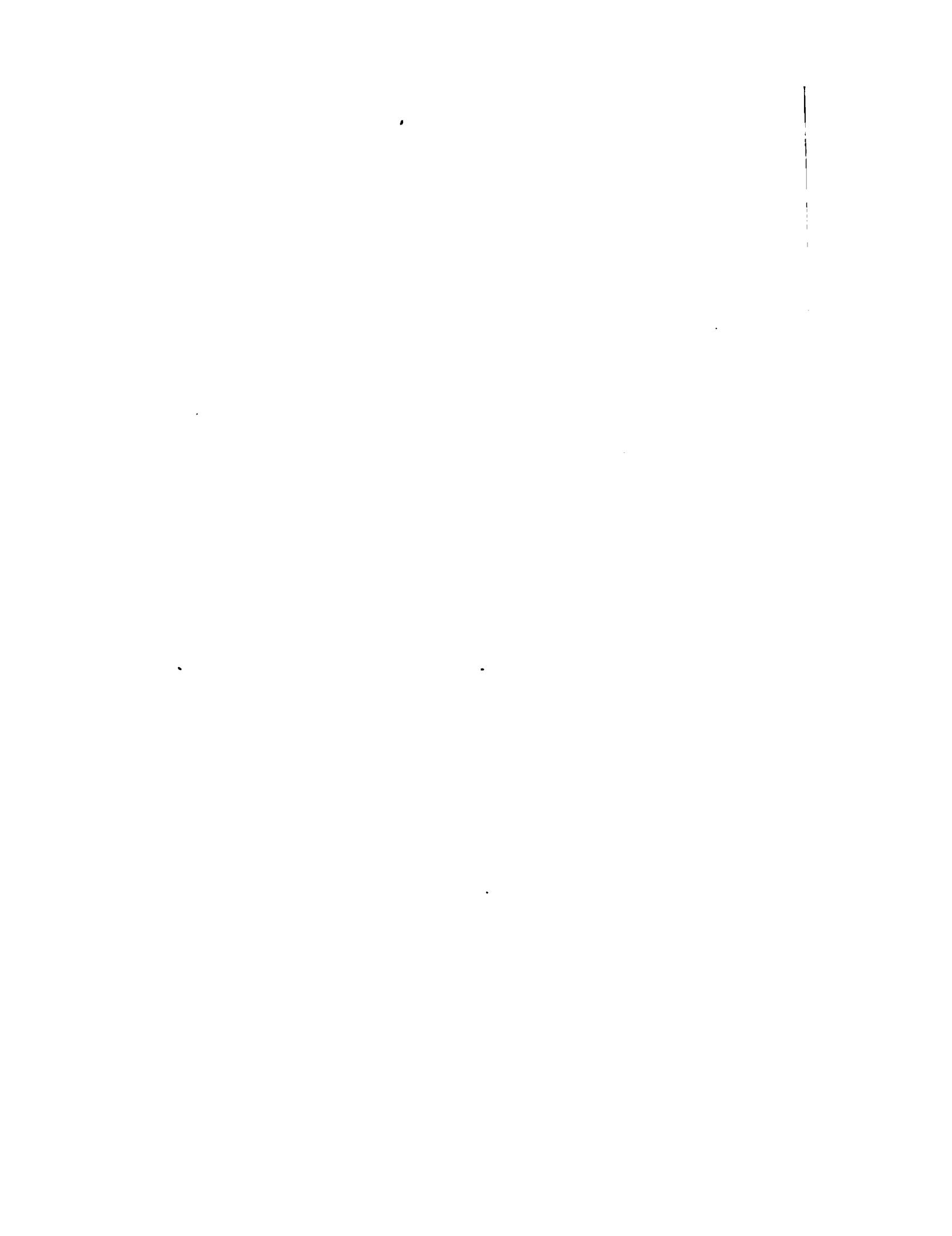
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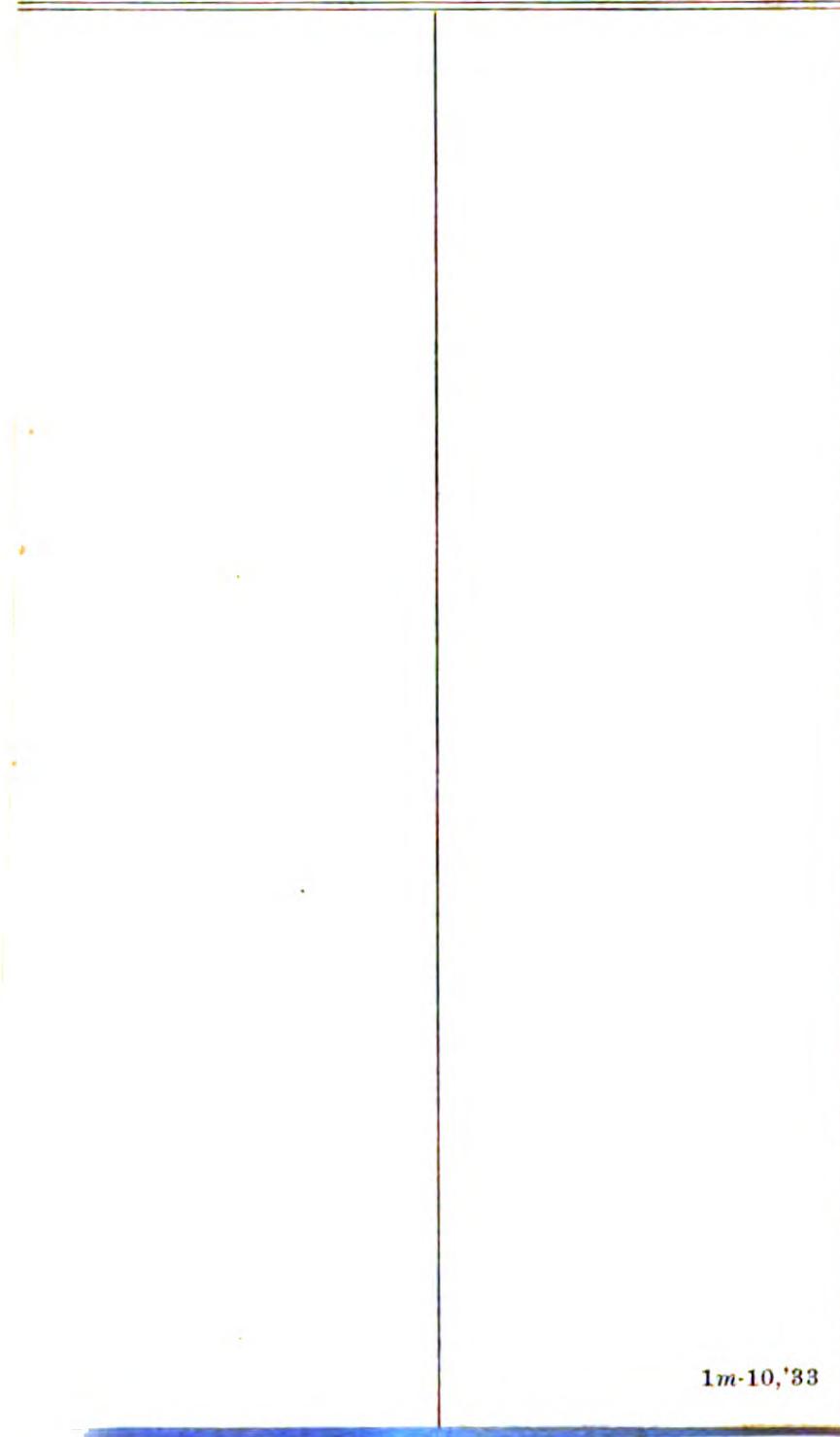


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